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(71) Applicant: **Eisai R&D Management Co., Ltd.**
Tokyo 112-8088 (JP)

(72) Inventor: **YAMAMOTO, Yuji**
Tsukuba-shi, Ibaraki 3002635 (JP)

(74) Representative: **Woods, Geoffrey Corlett et al**
J.A. KEMP & CO.
14 South Square
Gray's Inn
London
WC1R 5JJ (GB)

(54) USE OF COMBINATION OF ANTI-ANGIOGENIC SUBSTANCE AND c-kit KINASE INHIBITOR

(57) The object of the present invention is to find a pharmaceutical composition and a method for treating cancer that show an excellent antitumor effect. Combinational use of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide and analogues thereof can result in an excellent antitumor effect when combined with a substance having a c-kit kinase-inhibiting activity.

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Description

FIELD OF THE INVENTION

[0001] The present invention relates to a pharmaceutical composition and a kit comprising a combination of a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof (hereinafter, also referred to as a "compound of the invention") and a substance having a c-kit kinase-inhibiting activity (hereinafter, also referred to as a "c-kit inhibitor"), to a method for treating cancer comprising administering an effective amount of the pharmaceutical composition to a patient, to use of the compound of the invention for producing the pharmaceutical composition, and to the compound of the invention used for the pharmaceutical composition.

BACKGROUND OF THE INVENTION

[0002] Examples of conventionally used chemotherapeutic agents for cancer include alkylating agents such as cyclophosphamide, antimetabolites such as methotrexate and fluorouracil, antibiotics such as adriamycin, mitomycin and bleomycin, plant-derived taxol, vincristine and etoposide and metal complexes such as cisplatin. None of them, however, provides sufficient antitumor effect, and thus development of a novel antitumor drug has been strongly desired.

[0003] Recently, 4-(4-methylpiperazine-l-ylmethyl)-N-[4-methyl-3-[4-(3-pyridyl)pyrimidine-2-ylamino]phenyl]benzenamide (hereinafter, also referred to as "imatinib" or "STI571") is known as a c-kit inhibitor (Documents 1 and 2).

[0004] In addition, 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide is known as a VEGF receptor kinase inhibitor (Document 3-4).

[0005] However, it has not been elucidated yet what kind of antitumor effect can or cannot be obtained with a pharmaceutical composition containing a combination of these substances.

Documents

[0006]

1. Blood., 96, 925-932, 2000.
2. J Clin Oncol., 20, 1692-1703, 2002.
3. International publication No. 02/32872 (pamphlet)
4. International publication No. 2005/063713 (pamphlet)

DISCLOSURE OF THE INVENTION

[0007] The present invention was achieved regarding the circumstances described above. The problem to be solved by the invention is to find a pharmaceutical composition having an excellent antitumor effect and a method for treating cancer.

[0008] In order to solve the above problem, the present inventors have gone through keen examination, as a result of which combined use of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide and c-kit inhibitor imatinib was found to show an excellent antitumor effect.

[0009] Thus, the present invention relates to:

(1) a pharmaceutical composition comprising a combination of a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof and a substance having a c-kit kinase-inhibiting activity.

(2) A kit comprising: (a) at least one selected from the group consisting of a package, an instruction and an attached document describing combined use of a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof and a substance having a c-kit kinase-inhibiting activity; and (b) a pharmaceutical composition comprising a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof.

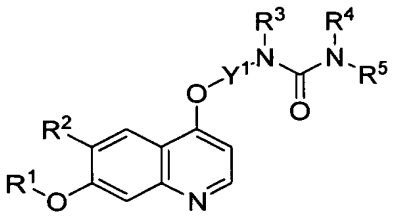
(3) A kit comprising a set of a formulation containing a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof, and a formulation containing a substance having a c-kit kinase-inhibiting activity.

(4) A pharmaceutical composition comprising a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof , which is administered to a patient with a substance having a c-kit kinase-inhibiting activity.

(5) A method for treating cancer comprising administering an effective amount of a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof and an effective amount of a substance

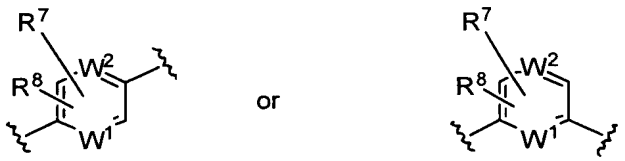
having a c-kit kinase-inhibiting activity to a patient.
(6) Use of a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof for producing a pharmaceutical composition in combination with a substance having a c-kit kinase-inhibiting activity.
(7) A compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof used for a pharmaceutical composition in combination with a substance having a c-kit kinase-inhibiting activity.

[0010] The compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is as follows:



(I)

[wherein, R^1 represents group represented by Formula $-V^1-V^2-V^3$ (wherein, V^1 represents C_{1-6} alkylene group that may have a substituent; V^2 represents a single bond, an oxygen atom, a sulfur atom, carbonyl group, sulfinyl group, sulfonyl group, group represented by Formula $-CONR^6-$, group represented by Formula $-SO_2NR^6-$, group represented by Formula $-NR^6SO_2-$, group represented by Formula $-NR^6CO-$ or group represented by Formula $-NR^6-$ (wherein, R^6 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent or C_{3-8} cycloalkyl group that may have a substituent); V^3 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent);
R^2 represents cyano group, C_{1-6} alkoxy group that may have a substituent, carboxyl group, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{a11}V^{a12}$ (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent);
Y^1 represents group represented by Formula



(wherein, R^7 and R^8 each independently represent a hydrogen atom, a halogen atom, cyano group, nitro group, amino group, C_{1-6} alkyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{1-6} alkoxy group that may have a substituent, C_{1-6} alkylthio group that may have a substituent, formyl group, C_{2-7} acyl group that may have a substituent, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{d1}V^{d2}$ (wherein, V^{d1} and V^{d2} each independently represent a hydrogen atom or C_{1-6} alkyl group that may have a substituent);
W^1 and W^2 each independently represent a carbon atom or a nitrogen atom that may have a substituent);
R^3 and R^4 each independently represent a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6}

alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{2-7} acyl group that may have a substituent or C_{2-7} alkoxycarbonyl group that may have a substituent;
R^5 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent].

[0011] Furthermore, the present invention preferably relates to the followings.

(1) A pharmaceutical composition comprising a combination of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarbox amide, a pharmacologically acceptable salt thereof or a solvate thereof and imatinib.
(2) A kit comprising: (a) at least one selected from the group consisting of a package, an instruction and an attached document describing combined use of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarbox amide, a pharmacologically acceptable salt thereof or a solvate thereof and imatinib; and (b) a pharmaceutical composition comprising 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarbox amide, a pharmacologically acceptable salt thereof or a solvate thereof.
(3) A kit comprising a set of a formulation containing 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide, a pharmacologically acceptable salt thereof or a solvate thereof and a formulation containing imatinib.
(4) A pharmaceutical composition comprising 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide, a pharmacologically acceptable salt thereof or a solvate thereof which is administered to a patient together with imatinib.
(5) A method for treating cancer comprising administering an effective amount of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide, a pharmacologically acceptable salt thereof or a solvate thereof and an effective amount of imatinib to a patient.
(6) Use of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide, a pharmacologically acceptable salt thereof or a solvate thereof for producing a pharmaceutical composition in combination with imatinib.
(7) 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide, a pharmacologically acceptable salt thereof or a solvate thereof for producing a pharmaceutical composition in combination with imatinib.

[0012] According to the present invention, a pharmaceutical composition comprising a combination of a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof and a c-kit inhibitor is provided, which can be used for treating cancer.

BRIEF DESCRIPTION OF DRAWINGS

[0013]

Figure 1 shows the combined effect of a VEGF receptor kinase inhibitor and a c-kit inhibitor in a human cancer cell line subcutaneous xenograft model. In Figure 1, Compound A refers to 4-(3-chloro-4-(cyclopropylaminocarbonyl) aminophenoxy)-7-methoxy-6-quinolinecarbo xamide and Compound B refers to imatinib.
Figure 2 shows the combined effect of a VEGF receptor kinase inhibitor and a c-kit inhibitor in a human cancer cell line subcutaneous xenograft model. In Figure 2, Compound A refers to 4-(3-chloro-4-(cyclopropylaminocarbonyl) aminophenoxy)-7-methoxy-6-quinolinecarbo xamide and Compound B refers to imatinib.

BEST MODES FOR CARRYING OUT THE INVENTION

[0014] Hereinafter, embodiments of the present invention will be described. The following embodiments illustrate the present invention, which are not intended to limit the present invention. The present invention may be carried out in various embodiments without departing from the scope of the invention.

[0015] The documents, laid-open patent applications, patent publications and other patent documents cited herein are incorporated herein by reference. The present specification incorporates the content of specification of Japanese Patent Application No. 2005-322946 based on which the present application claims priority.

1. Compound

[0016] Herein, "a halogen atom" refers to a fluorine atom, a chlorine atom, a bromine atom or an iodine atom.

[0017] Preferable examples of "a halogen atom" include a fluorine atom and a chlorine atom.

[0018] Herein, "C_{1-6} alkyl group" refers to linear or branched alkyl group with a carbon number of 1-6, and specific examples include methyl group, ethyl group, 1-propyl group (n-propyl group), 2-propyl group (i-propyl group), 2-methyl-1-propyl group (i-butyl group), 2-methyl-2-propyl group (t-butyl group), 1-butyl group (n-butyl group), 2-butyl group (s-butyl group), 1-pentyl group, 2-pentyl group, 3-pentyl group, 2-methyl-1-butyl group, 3-methyl-1-butyl group, 2-methyl-2-butyl group, 3-methyl-2-butyl group, 2,2-dimethyl-1-propyl group , 1-hexyl group, 2- hexyl group, 3- hexyl group, 2-methyl-1-pentyl group, 3-methyl-1-pentyl group, 4-methyl-1-pentyl group, 2-methyl-2-pentyl group, 3-methyl-2-pentyl group, 4-methyl-2-pentyl group, 2-methyl-3-pentyl group, 3-methyl-3-pentyl group, 2,3-dimethyl-1-butyl group, 3,3-dimethyl-1-butyl group, 2,2-dimethyl-1-butyl group, 2-ethyl-1-butyl group, 3,3-dimethyl-2-butyl group and 2,3-dimethyl-2-butyl group.

[0019] Preferable examples of "C_{1-6} alkyl group" include methyl group, ethyl group, 1-propyl group , 2-propyl group , 2-methyl-1-propyl group , 2-methyl-2-propyl group , 1-butyl group and 2-butyl group.

[0020] Herein, "C_{1-6} alkylene group" refers to divalent group derived from the "C_{1-6} alkyl group" defined above by removing any one hydrogen atom therefrom, and specific examples include methylene group, 1,2-ethylene group, 1,1-ethylene group, 1,3-propylene group, tetramethylene group, pentamethylene group and hexamethylene group.

[0021] Herein, "C_{2-6} alkenyl group" refers to linear or branched alkenyl group having one double bond and a carbon number of 2-6, and specific examples include ethenyl group (vinyl group), 1-propenyl group, 2-propenyl group (allyl group), 1-butenyl group, 2-butenyl group, 3-butenyl group, pentenyl group and hexenyl group.

[0022] Herein, "C_{2-6} alkynyl group" refers to linear or branched alkynyl group having one triple bond and a carbon number of 2-6, and specific examples include ethinyl group, 1-propynyl group, 2-propynyl group, 1-butynyl group, 2-butynyl group, 3-butynyl group, pentynyl group and hexynyl group.

[0023] Herein, "C_{3-8} cycloalkyl group" refers to monocyclic or bicyclic saturated aliphatic hydrocarbon group with a carbon number of 3-8, and specific examples include cyclopropyl group , cyclobutyl group, cyclopentyl group, cyclohexyl group, cycloheptyl group, cyclooctyl group, bicyclo[2. 1. 0]pentyl group, bicyclo[3. 1. 0]hexyl group, bicyclo[2. 1. 1]hexyl group, bicyclo[4. 1. 0]heptyl group, bicyclo[2. 2. 1]heptyl group (norbornyl group), bicyclo[3. 3. 0]octyl group, bicyclo[3. 2. 1]octyl group and bicyclo[2. 2. 2]octyl group.

[0024] Preferable examples of "C_{3-8} cycloalkyl group" include cyclopropyl group, cyclobutyl group and cyclopentyl group.

[0025] Herein, "C_{6-10} aryl group" refers to aromatic hydrocarbon cyclic group with a carbon number of 6-10, and specific examples include phenyl group, 1-naphthyl group, 2-naphthyl group, indenyl group and azulenyl group.

[0026] A preferable example of "C_{6-10} aryl group" includes phenyl group.

[0027] Herein, "a heteroatom" refers to a nitrogen atom, an oxygen atom or a sulfur atom.

[0028] Herein, "5-10-membered heteroaryl group" refers to aromatic cyclic group having 5-10 atoms forming the ring and 1-5 heteroatoms included in the atom forming the ring, and specific examples include furyl group, thienyl group, pyrrolyl group, imidazolyl group, triazolyl group, tetrazolyl group, thiazolyl group, pyrazolyl group, oxazolyl group, isoxazolyl group, isothiazolyl group, furazanyl group, thiadiazolyl group, oxadiazolyl group, pyridyl group, pyrazinyl group, pyridazinyl group, pyrimidinyl group, triazinyl group, purinyl group, pteridinyl group, quinolyl group, isoquinolyl group, naphthiridinyl group, quinoxalinyl group, cinnolinyl group, quinazolinyl group, phthalazinyl group, imidazopyridyl group, imidazothiazolyl group, imidazoxazolyl group, benzothiazolyl group, benzoxazolyl group, benzimidazolyl group, indolyl group, isoindolyl group, indazolyl group, pyrrolopyridyl group, thienopyridyl group, furopyridyl group, benzothiadiazolyl group, benzoxadiazolyl group, pyridopyrimidinyl group, benzofuryl group, benzothienyl group and thienofuryl group.

[0029] Preferable examples of "5-10-membered heteroaryl group" include furyl group, thienyl group, pyrrolyl group, imidazolyl group, thiazolyl group, pyrazolyl group, oxazolyl group, isoxazolyl group, isothiazolyl group, pyridyl group and pyrimidinyl group.

[0030] Herein, "3-10-membered nonaromatic heterocyclic group":

(1) has 3-10 atoms forming the ring;
(2) has 1-2 heteroatoms included in the atoms forming the ring;
(3) may include 1-2 double bonds in the ring;
(4) may have 1-3 carbonyl group, sulfinyl group or sulfonyl group in the ring; and
(5) is nonaromatic monocyclic or bicyclic group. When a nitrogen atom is included in the atoms forming the ring, the nitrogen atom may have a binding hand. Specific examples include aziridinyl group, azetidinyl group, pyrrolidinyl group, piperidinyl group, azepanyl group, azocanyl group, piperazinyl group, diazepanyl group, diazocanyl group, diazabicyclo[2. 2. 1]heptyl group, morpholinyl group, thiomorpholinyl group, 1,1-dioxothiomorpholinyl group, oxiranyl group, oxetanyl group, tetrahydrofuryl group, dioxoranyl group, tetrahydropyranyl group, dioxanyl group, tetrahy-

drothienyl group, tetrahydrothiopyranyl group, oxazolidinyl group and thiazolidinyl group.

[0031] Preferable examples of "3-10-membered nonaromatic heterocyclic group" include aziridinyl group, azetidinyl group, pyrrolidinyl group, piperidinyl group, azepanyl group, piperazinyl group, diazepanyl group, morpholinyl group, thiomorpholinyl group, 1,1-dioxothiomorpholinyl group, tetrahydrofuryl group and tetrahydropyranyl group.

[0032] Herein, "C_{1-6} alkoxy group" refers to group in which an oxygen atom is bound to the terminal of "C_{1-6} alkyl group" defined above, and specific examples include methoxy group, ethoxy group, 1-propoxy group (n-propoxy group), 2-propoxy group (i-propoxy group), 2-methyl-1-propoxy group (i-butoxy group), 2-methyl-2-propoxy group (t-butoxy group), 1-butoxy group (n-butoxy group), 2-butoxy group (s-butoxy group), 1-pentyloxy group, 2-pentyloxy group, 3-pentyloxy group, 2-methyl-1-butoxy group, 3-methyl-1-butoxy group, 2-methyl-2-butoxy group, 3-methyl-2-butoxy group, 2,2-dimethyl-1-propoxy group, 1-hexyloxy group, 2-hexyloxy group, 3-hexyloxy group, 2-methyl-1-pentyloxy group, 3-methyl-1-pentyloxy group, 4-methyl-1-pentyloxy group, 2-methyl-2-pentyloxy group, 3-methyl-2-pentyloxy group, 4-methyl-2-pentyloxy group, 2-methyl-3-pentyloxy group, 3-methyl-3-pentyloxy group, 2,3-dimethyl-1-butoxy group, 3,3-dimethyl-1-butoxy group, 2,2-dimethyl-1-butoxy group, 2-ethyl-1-butoxy group, 3,3-dimethyl-2-butoxy group and 2,3-dimethyl-2-butoxy group.

[0033] Preferable examples of "C_{1-6} alkoxy group" include methoxy group, ethoxy group, 1-propoxy group, 2-propoxy group, 2-methyl-1-propoxy group, 2-methyl-2-propoxy group, 1-butoxy group and 2-butoxy group.

[0034] Herein, "C_{1-6} alkylthio group" refers to group in which a sulfur atom is bound to the terminal of "C_{1-6} alkyl group" defined above, and specific examples include methylthio group, ethylthio group, 1-propylthio group (n-propylthio group), 2-propylthio group (i-propylthio group), 2-methyl-1-propylthio group (i-butylthio group), 2-methyl-2-propylthio group (t-butylthio group), 1-butylthio group (n-butylthio group), 2-butylthio group (s-butylthio group), 1-pentylthio group, 2-pentylthio group, 3-pentylthio group, 2-methyl-1-butylthio group, 3-methyl-1-butylthio group, 2-methyl-2-butylthio group, 3-methyl-2-butylthio group, 2,2-dimethyl-1-propylthio group, 1-hexylthio group, 2-hexylthio group, 3-hexylthio group, 2-methyl-1-pentylthio group, 3-methyl-1-pentylthio group, 4-methyl-1-pentylthio group, 2-methyl-2-pentylthio group, 3-methyl-2-pentylthio group, 4-methyl-2-pentylthio group, 2-methyl-3-pentylthio group, 3-methyl-3-pentylthio group, 2,3-dimethyl-1-butylthio group, 3,3-dimethyl-1-butylthio group, 2,2-dimethyl-1-butylthio group, 2-ethyl-1-butylthio group, 3,3-dimethyl-2-butylthio group and 2,3-dimethyl-2-butylthio group.

[0035] Preferable examples of "C_{1-6} alkylthio group" include methylthio group, ethylthio group, 1-propylthio group (n-propylthio group), 2-propylthio group (i-propylthio group), 2-methyl-1-propylthio group (i-butylthio group), 2-methyl-2-propylthio group (t-butylthio group), 1-butylthio group (n-butylthio group) and 2-butylthio group (s-butylthio group).

[0036] Herein, "C_{3-8} cycloalkoxy group" refers to group in which an oxygen atom is bound to the terminal of "C_{3-8} cycloalkyl group" defined above, and specific examples include cyclopropoxy group, cyclobutoxy group, cyclopentyloxy group, cyclohexyloxy group, cycloheptyloxy group, cyclooctyloxy group, bicyclo[2. 1. 0]pentyloxy group, bicyclo[3. 1. 0]hexyloxy group, bicyclo[2. 1. 1]hexyloxy group, bicyclo[4. 1. 0]heptyloxy group, bicyclo[2. 2. 1]heptyloxy group (norbornyloxy group), bicyclo[3. 3. 0]octyloxy group, bicyclo[3. 2. 1]octyloxy group and bicyclo[2. 2. 2]octyloxy group.

[0037] Preferable examples of "C_{3-8} cycloalkoxy group" include cyclopropoxy group, cyclobutoxy group and cyclopentyloxy group.

[0038] Herein, "mono-C_{1-6} alkylamino group" refers to group in which a hydrogen atom in amino group is substituted with "C_{1-6} alkyl group" defined above, and specific examples include methylamino group, ethylamino group, 1-propylamino group (n-propylamino group), 2-propylamino group (i-propylamino group), 2-methyl-1-propylamino group (i-butylamino group), 2-methyl-2-propylamino group (t-butylamino group), 1-butylamino group (n-butylamino group), 2-butylamino group (s-butylamino group), 1-pentylamino group, 2-pentylamino group, 3-pentylamino group, 2-methyl-1-butylamino group, 3-methyl-1-butylamino group, 2-methyl-2-butylamino group, 3-methyl-2-butylamino group, 2,2-dimethyl-1-propylamino group, 1-hexylamino group, 2-hexylamino group, 3-hexylamino group, 2-methyl-1-pentylamino group, 3-methyl-1-pentylamino group, 4-methyl-1-pentylamino group, 2-methyl-2-pentylamino group, 3-methyl-2-pentylamino group, 4-methyl-2-pentylamino group, 2-methyl-3-pentylamino group, 3-methyl-3-pentylamino group, 2,3-dimethyl-1-butylamino group, 3,3-dimethyl-1-butylamino group, 2,2-dimethyl-1-butylamino group, 2-ethyl-1-butylamino group, 3,3-dimethyl-2-butylamino group and 2,3-dimethyl-2-butylamino group.

[0039] Herein, "di-C_{1-6} alkylamino group" refers to group in which two hydrogen atoms in amino group are substituted with identical or different "C_{1-6} alkyl group" defined above, and specific examples include N,N-dimethylamino group, N,N-diethylamino group, N,N-di-n-propylamino group, N,N-di-i-propylamino group, N,N-di-n-butylamino group, N,N-di-i-butylamino group, N,N-di-s-butylamino group, N,N-di-t-butylamino group, N-ethyl-N-methylamino group, N-n-propyl-N-methylamino group, N-i-propyl-N-methylamino group, N-n-butyl-N-methylamino group, N-i-butyl-N-methylamino group, N-s-butyl-N-methylamino group and N-t-butyl-N-methylamino group.

[0040] Herein, "C_{2-7} acyl group" refers to carbonyl group bound with "C_{1-6} alkyl group" defined above, and specific examples include acetyl group, propionyl group, isopropionyl group, butyryl group, isobutyryl group, valeryl group, isovaleryl group and pivaloyl group.

[0041] Herein, "C_{2-7} alkoxycarbonyl group" refers to carbonyl group bound with "C_{1-6} alkoxy group" defined above,

and specific examples include methoxycarbonyl group, ethoxycarbonyl group, 1-propyloxycarbonyl group, 2-propyloxycarbonyl group and 2-methyl-2-propoxy group.

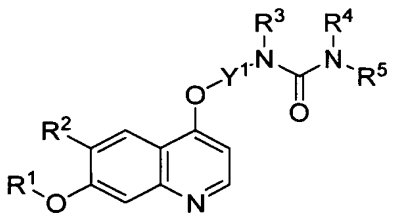
[0042] Herein, "that may have a substituent" means "that may have one or more substituents in any combination at substitutable positions", and specific examples include a halogen atom, hydroxyl group, thiol group, nitro group, cyano group, formyl group, carboxyl group, amino group, silyl group, methanesulfonyl group, C_{1-6} alkyl group, C_{2-6} alkenyl group, C_{2-6} alkynyl group, C_{3-8} cycloalkyl group, C_{6-10} aryl group, 5-10-membered heteroaryl group, 3-10-membered nonaromatic heterocyclic group, C_{1-6} alkoxy group, C_{1-6} alkylthio group, C_{3-8} cycloalkoxy group, mono-C_{1-6} alkylamino group, di-C_{1-6} alkylamino group, C_{2-7} acyl group and C_{2-7} alkoxycarbonyl group. In this case, C_{1-6} alkyl group, C_{2-6} alkenyl group, C_{2-6} alkynyl group, C_{3-8} cycloalkyl group, C_{6-10} aryl group, 5-10-membered heteroaryl group, 3-10-membered nonaromatic heterocyclic group, C_{1-6} alkoxy group, C_{1-6} alkylthio group, C_{3-8} cycloalkoxy group, mono-C_{1-6} alkylamino group, di-C_{1-6} alkylamino group, C_{2-7} acyl group and C_{2-7} alkoxycarbonyl group may each independently have 1-3 groups selected from the group consisting from the following substituent groups.

<Substituent groups>

[0043] A halogen atom, hydroxyl group, thiol group, nitro group, cyano group, C_{1-6} alkyl group, C_{3-8} cycloalkyl group, C_{2-6} alkenyl group, C_{2-6} alkynyl group, C_{6-10} aryl group, 5-10-membered heteroaryl group, 3-10-membered nonaromatic heterocyclic group, C_{1-6} alkoxy group and C_{1-6} alkylthio group.

(A) Compound of the invention

[0044] According to the present invention, compound represented by Formula (I) is as follows.



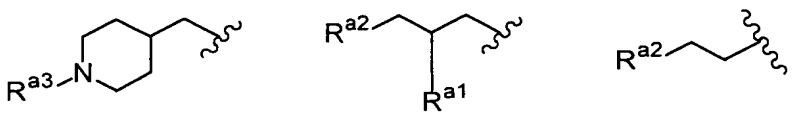
(I)

(i) R^1

[0045] R^1 represents group represented by Formula $-V^1-V^2-V^3$ (wherein, V^1 represents C_{1-6} alkylene group that may have a substituent; V^2 represents a single bond, an oxygen atom, a sulfur atom, carbonyl group, sulfinyl group, sulfonyl group, group represented by Formula $-CONR^6-$, group represented by Formula $-SO_2NR^6-$, group represented by Formula $-NR^6SO_2-$, group represented by Formula $-NR^6CO-$ or group represented by Formula $-NR^6-$ (wherein, R^6 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent or C_{3-8} cycloalkyl group that may have a substituent); V^3 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent).

[0046] A preferable example of R^1 includes C_{1-6} alkyl group. In this case, R^1 may have a substituent selected from 3-10-membered nonaromatic heterocyclic group which may have C_{1-6} alkyl group, hydroxyl group, C_{1-6} alkoxy group, amino group, mono-C_{1-6} alkylamino group and di-C_{1-6} alkylamino group.

[0047] More preferable examples of R^1 include methyl group and group represented by any one of Formulae



(wherein, R^{a3} represents methyl group; R^{a1} represents a hydrogen atom or hydroxyl group; R^{a2} represents methoxy

group, ethoxy group, 1-pyrrolidinyl group, 1-piperidinyl group, 4-morpholinyl group, dimethylamino group or diethylamino group).

[0048] Still more preferable examples of R^1 include methyl group and 2-methoxyethyl group.

(ii) R^2

[0049] R^2 represents cyano group, C_{1-6} alkoxy group that may have a substituent, carboxyl group, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula -$CONV^{a11}V^{a12}$ (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent).

[0050] Preferable examples of R^2 include cyano group or group represented by Formula- $CONV^{a11}V^{a12}$ (wherein, V^{a11} and V^{a12} have the same meaning as defined above).

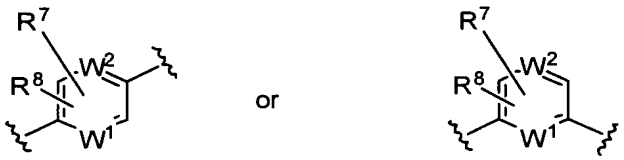
[0051] More preferable examples of R^2 include cyano group or group represented by Formula -$CONHV^{a16}$ (wherein, V^{a16} represents a hydrogen atom, C_{1-6} alkyl group, C_{3-8} cycloalkyl group, C_{1-6} alkoxy group or C_{3-8} cycloalkoxy group, where V^{a16} may have a substituent selected from a halogen atom, cyano group, hydroxyl group and C_{1-6} alkoxy group).

[0052] Still more preferable example of R^2 includes group represented by Formula -$CONHV^{a17}$ (wherein, V^{a17} represents a hydrogen atom, C_{1-6} alkyl group or C_{1-6} alkoxy group).

[0053] The most preferable example of R^2 include group represented by Formula -$CONHV^{a18}$ (wherein, V^{a18} represents a hydrogen atom, methyl group or methoxy group).

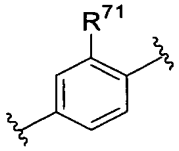
(iii) Y^1

[0054] Y^1 represents group represented by Formula



(wherein, R^7 and R^8 each independently represent a hydrogen atom, a halogen atom, cyano group, nitro group, amino group, C_{1-6} alkyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{1-6} alkoxy group that may have a substituent, C_{1-6} alkylthio group that may have a substituent, formyl group, C_{2-7} acyl group that may have a substituent, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula -$CONV^{d1}V^{d2}$ (wherein, V^{d1} and V^{d2} each independently represent a hydrogen atom or C_{1-6} alkyl group that may have a substituent); and W^1 and W^2 each independently represent a carbon atom or a nitrogen atom that may have a substituent).

[0055] A preferable example of Y^1 includes group represented by Formula



(wherein, R^{71} represents a hydrogen atom or a halogen atom).

(iv) R^3 and R^4

[0056] R^3 and R^4 each independently represent a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{2-7} acyl group that may have a substituent or C_{2-7} alkoxycarbonyl group that may have a substituent.

[0057] A preferable example of R^3 and R^4 includes a hydrogen atom.

(v) R^5

[0058] R^5 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent.

[0059] Preferable examples of R^5 include a hydrogen atom, C_{1-6} alkyl group, C_{3-8} cycloalkyl group and C_{6-10} aryl group (where R^5 may have a substituent selected from a halogen atom and methanesulfonyl group).

[0060] More preferable examples of R^5 include methyl group, ethyl group or cyclopropyl group.

[0061] Moreover, preferable examples of the compound represented by Formula (I) include:

N-(4-(6-cyano-7-(2-methoxyethoxy)-4-quinolyl)oxy-2-fluorophenyl)-N'-(4-fluorophenyl)urea;
N-(2-chloro-4-((6-cyano-7-((1-methyl-4-piperidyl)methoxy)-4-quinolyl)oxy)phenyl)-N'-cyclopropylurea;
N-(4-((6-cyano-7-(((2R)-3-(diethylamino)-2-hydroxypropyl)oxy)-4-quinolyl)oxy)phenyl)-N'-(4-fluorophenyl)urea;
N-(4-((6-cyano-7-(((2R)-2-hydroxy-3-(1-pyrrolidino)propyl)oxy)-4-quinolyl)oxy)phenyl)-N'-(4-fluorophenyl)urea;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N6-cyclopropyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-methoxyethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-fluoroethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methoxy-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-ethyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-hydroxyethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-((2S)-2,3-dihydroxypropyl)oxy-6-quinolinecarboxamide;
4-(3-chloro-4-(methylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methoxy-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-ethoxyethoxy)-6-quinolinecarboxamide;
4-(4-((cyclopropylamino)carbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N-(2-fluoro-4-((6-carbamoyl-7-methoxy-4-quinolyl)oxy)phenyl)-N'-cyclopropylurea;
N6-(2-hydroxyethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(1-propylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cis-2-fluoro-cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-(4-morpholino)ethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(2-fluoroethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-((2R)tetrahydro-2-furanylmethyl)-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino)propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-((2R)-3-diethylamino-2-hydroxypropoxy)-6-

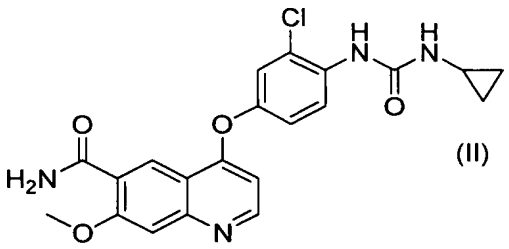
quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((2R)-3-diethylamino-2-hydroxypropoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino)propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino)propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-((1-methyl-4-piperidyl)methoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((1-methyl-4-piperidyl)methoxy)-6-quinolinecarboxamide;
N-(4-(6-cyano-7-(2-methoxyethoxy)-4-quinolyl)oxy-2-fluorophenyl)-N'-cyclopropylurea;
N-(4-(6-cyano-7-(3-(4-morpholino)propoxy)-4-quinolyl)oxyphenyl)-N'-(3-(methylsulfonyl)phenyl)urea;
4-(4-((cyclopropylamino)carbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-((2-fluoroethylamino)carbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-ethoxyethyl)-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(4-(3-ethylureido)-3-fluoro-phenoxy)-7-methoxyquinoline-6-carboxylic acid (2-cyanoethyl)amide; and
N-(4-(6-(2-cyanoethyl)carbamoyl-7-methoxy-4-quinolyl)oxy-2-fluorophenyl)-N'-cyclopropylurea.

[0062] More preferable examples of the compound represented by Formula (I) further include:

4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methoxy-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(methylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide; and
N6-methoxy-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide.

[0063] A still more preferable example of the compound represented by Formula (I) further includes 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide (see Formula (II)).

[0064] The most preferable example of the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof includes methanesulfonate of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide.



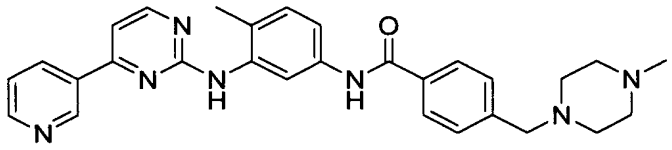
(II)

[0065] The compound represented by Formula (I) can be produced by a known method, for example, by methods described in International publication No. 02/32872 pamphlet (WO02/32872) and International publication No. 2005/063713 pamphlet (WO2005/063713).

(B) C-kit inhibitor

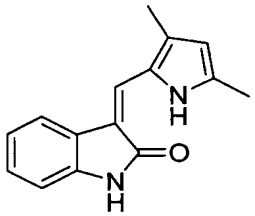
[0066] According to the present invention, examples of the c-kit inhibitor include:

(1) 4-(4-methylpiperazine-1-ylmethyl)-N-[4-methyl-3-[4-(3-pyridyl)pyrimidine-2-ylamino]phenyl]benzenamide (hereinafter, also referred to as "imatinib" or "STI571". Blood., 96, 925-932, 2000., Bioorganic and Medicinal Chemistry Letters., 7: 187-192, 1997) (see Formula (III))



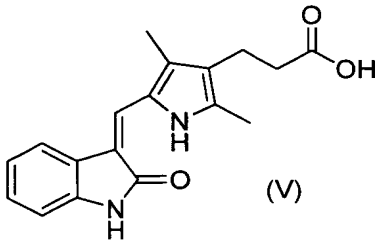
(III) ;

(2) 3-[(2,4-dimethylpyrrole-5-yl)methylene]-2-indolinone (hereinafter, also referred to as "SU5416" or "semaxanib". Cancer Research., 61, 3660-3668, 2000, Journal of Medicinal Chemistry., 41: 2588-2603, 1998., US5792783) (see Formula (IV))



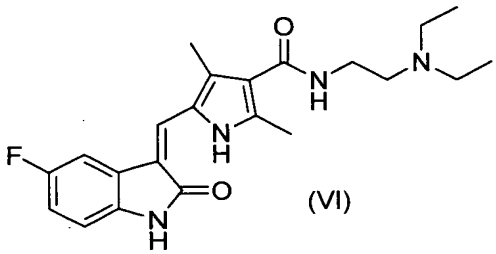
(IV) ;

(3) (Z)-3-[(2,4-dimethyl-5-(2-oxo-1,2-dihydroindole-3-ylidenemethyl)-1H-pyrrole-3-yl)-propionic acid (hereinafter, also referred to as "SU6668". Cancer Research., 61, 3660-3668, 2000, Journal of Medicinal Chemistry., 42: 5120-5130, 1999.) (see Formula (V))



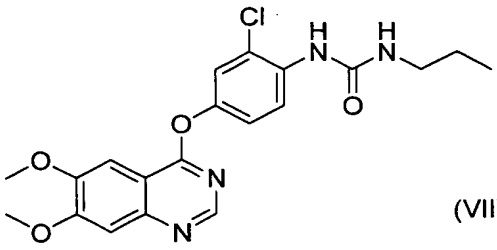
(V) ;

(4) 5-(5-fluoro-2-oxo-1,2-dihydroindole-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide (hereinafter, also referred to as "SU11248". Molecular Cancer Therapeutics., 2:471-478, 2003, Journal of Medicinal Chemistry., 46: 1116-9, 2003.) (see Formula (VI))



(VI) ;

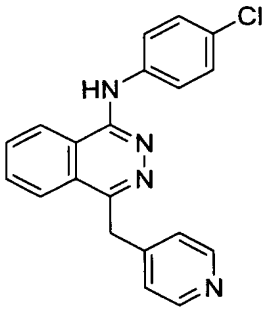
(5) N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-propylurea (hereinafter, also referred to as "KRN633". Molecular Cancer Therapeutics., 3:1639-49, 2004) (see Formula (VII))



(VII)

;

(6) 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine (hereinafter, also referred to as "PTK787/ZK222584" or "vatalanib". Cancer Research, 60, 2178-2189, 2000, Journal of Medicinal Chemistry., 43:2310-23, 2000., WO98/35958) (see Formula (VIII))



(VIII)

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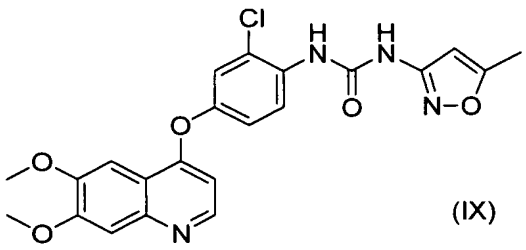
(7) N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea (hereinafter, also referred to as "KRN951". Proceedings of the American Association for Cancer Research, 45, 594, (Abstract 2571), 2004., Proceedings of the American Association for Cancer Research, 45, 595, (Abstract 2575), 2004., WO2002/088110) (see Formula (IX))



(IX)

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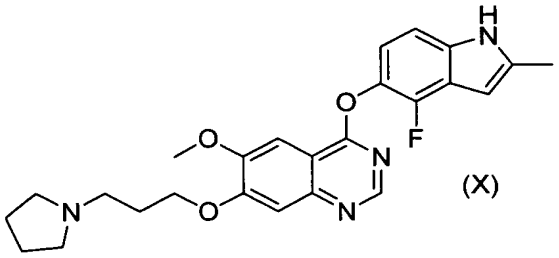
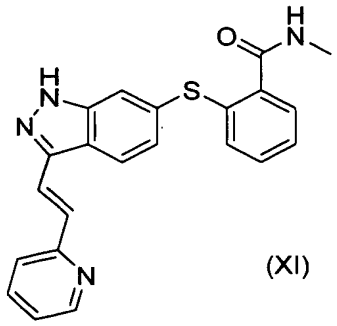
(8) 4-[(4-fluoro-2-methylindole-5-yl)oxy]-6-methoxy-7-[3-(pyrrolidine-l-yl)propoxy]quinazoline (hereinafter, also referred to as "AZD2171". Cancer Research. 65:4389-400, 2005, WO00/47212) (see Formula (X))



(X)

;

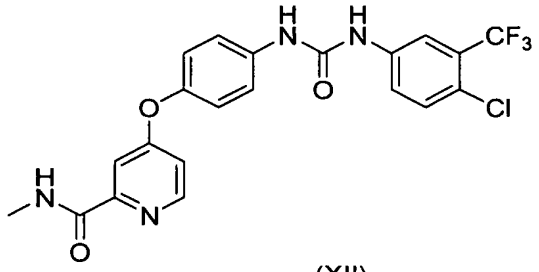
(9) 6-[2-(methylcarbamoyl)phenylsulfanil]-3-E-[2-(pyridine-2-yl)ethenyl]indazole (hereinafter, also referred to as "AG013736". Proceedings of the American Association for Cancer Research, 44, 865, (Abstract 3780), 2003, American Journal of Pathology. 165:35-52, 2004., WO01/002369) (see Formula (XI))



(XI)

;

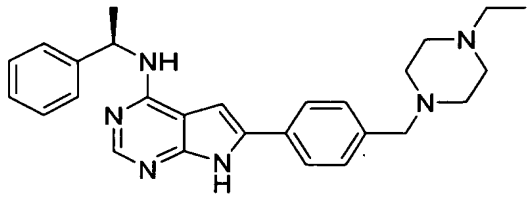
(10) N-(3-trifluoromethyl-4-chlorophenyl)-N'-(4-(2-methylcarbamoylpyridine-4-yl)oxyphenyl)urea (hereinafter, also referred to as "BAY 43-9006" or "sorafenib". Cancer Research., 64, 7099-7109, 2004, Organic Process Res Dev., 6, 777-81, 2002., WO00/42012) (see Formula (XII))



(XII)

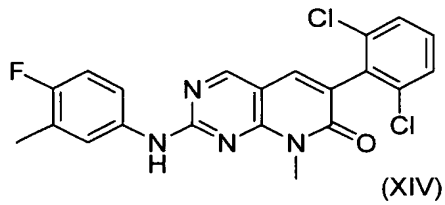
;

(11) [6-[4-[(4-ethylpiperazine-1-yl)methyl]phenyl]-7H-pyrrolo[2,3-d]pyrimidine-4-yl]-((R)-1-phenylethyl)amine (hereinafter, also referred to as "AEE-788". Cancer Research., 64, 4931-4941, 2004., Cancer Research., 64, 7977-7984, 2004.) (see Formula (XIII))



(XIII) ;

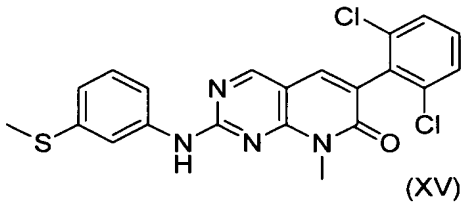
(12) 6-(2,6-dichloro-phenyl)-2-(4-fluoro-3-methyl-phenylamino)-8-methyl8H-pyrido[2,3-d]pyrimidine-7-one (hereinafter, also referred to as "PD180970". Cancer Research., 62, 4244-4255, 2002., Journal of Medicinal Chemistry., 40, 2296-2303, 1997.) (see Formula (XIV))



(XIV)

;

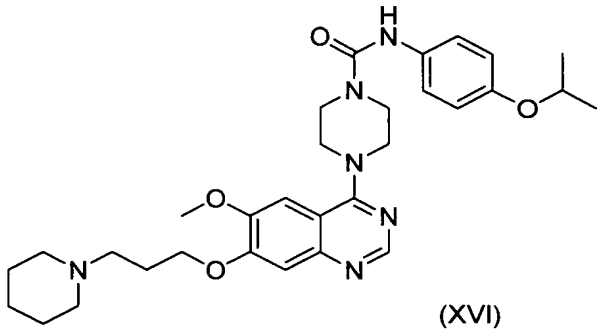
(13) 6-(2,6-dichlorophenyl)-8-methyl-2-(3-methylsulfanilphenylamino)-8H-pyrido[2,3-/d/]pyrimidine-7-one (hereinafter, also referred to as "PD173955". Cancer Research., 62, 4244-4255, 2002., Journal of Medicinal Chemistry., 40, 2296-2303, 1997.) (see Formula (XV))



(XV)

;

(14) 4-[6-methoxy-7-(3-piperidine-1-yl-propoxy)quinazoline-4-yl]piperazine-1-carboxylic acid(4-isopropoxyphenyl) amide (hereinafter, also referred to as "MLN518" or "tandutinib". Blood., 104, 3754-3757, 2004., Journal of Medicinal Chemistry., 45, 3772-3793, 2002.) (see Formula (XVI))

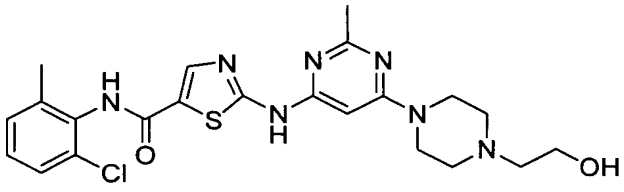


(XVI)

;

and

(15) N-(2-chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)piperazine-1-yl]-2-methylpyrimidine-4-yl]amino]thiazole-5-carboxamide (hereinafter, also referred to as "BMS-354825" or "dasatinib". Proceedings of the National Academy of Sciences of the United States of America., 102, 11011-11016, 2005.) (see Formula (XVII))



(XVII)

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[0067] Imatinib, SU5416, SU6668, SU11248, KRN633, PTK787/ZK222584, KRN951, AZD2171, AG013736, BAY 43-9006, AEE-788, PD180970, PD173955, MLN518 and BMS-354825 can be produced by a known method, for example, by methods described in the respective documents.

[0068] In addition, imatinib is available by purchasing Glivec™ from Novartis Pharma K.K..

[0069] According to the present invention, the compound represented by Formula (I) and/or the c-kit inhibitor may form a pharmacologically acceptable salt with acid or base. The compound represented by Formula (I) and/or the c-kit inhibitor of the invention also comprises such pharmacologically acceptable salts. Examples of salts formed with acid include inorganic acid salts such as hydrochloride, hydrobromate, sulfate and phosphate, and organic acid salts such as formic acid, acetic acid, lactic acid, succinic acid, fumaric acid, maleic acid, citric acid, tartaric acid, stearic acid, benzoic acid, methanesulfonic acid, benzenesulfonic acid, p-toluenesulfonic acid and trifluoroacetic acid. Examples of salts formed with base include alkali metal salts such as sodium salt and potassium salt, alkaline earth metal salts such as calcium salt and magnesium salt, organic base salts such as trimethylamine, triethylamine, pyridine, picoline, dicyclohexylamine, N, N'-dibenzyl ethylenediamine, arginine and lysine and ammonium salt.

[0070] Furthermore, according to the present invention, the compound represented by Formula (I) and/or the c-kit inhibitor also comprises, if any, solvates and enantiomers thereof. Examples of solvates include hydrates and nonhydrates, preferably hydrates. Examples of solvents include water, alcohols (for example, methanol, ethanol, n-propanol) and dimethylformamide.

[0071] Moreover, according to the present invention, the compound represented by Formula (I) may be crystalline or amorphous. If a crystalline polymorph is present, it may be a single product of any one of the crystal forms or a mixture of such forms.

[0072] According to the present invention, the compound of the invention and/or the c-kit inhibitor also comprises compounds that generate the compound represented by Formula (I) and/or the c-kit inhibitor by undergoing metabolism such as oxidation, reduction and hydrolysis *in vivo.*

[0073] According to the present invention, an example of the c-kit inhibitor includes an anti-c-kit kinase antibody.

[0074] According to the present invention, an anti-c-kit kinase antibody is an antibody that has affinity with c-kit kinase

or a partial fragment thereof. Preferably, an anti-c-kit kinase antibody is a neutralizing antibody that recognizes and binds with c-kit kinase to inhibit the vascular endothelial cell growth activity of c-kit kinase. According to the present invention, an anti-c-kit kinase antibody is, for example, a polyclonal antibody, a monoclonal antibody, a chimeric antibody, a single-chain antibody (scFV) (Huston et al. (1988) Proc. Natl. Acad. Sci. USA 85: 5879-83; The Pharmacology of Monoclonal Antibody, vol.113, Rosenburg and Moore ed., Springer Verlag (1994) pp.269-315), a humanized antibody, a polyspecific antibody (LeDoussal et al. (1992) Int. J. Cancer Suppl. 7: 58-62; Paulus (1985) Behring Inst. Mitt. 78: 118-32; Millstein and Cuello (1983) Nature 305: 537-9; Zimmermann (1986) Rev. Physiol. Biochem. Pharmacol. 105: 176-260; Van Dijk et al. (1989) Int. J. Cancer 43: 944-9), or antibody fragments such as Fab, Fab', F(ab')2, Fc and Fv, preferably a monoclonal antibody. Furthermore, if necessary, an anti-c-kit kinase antibody may be modified with polyethyleneglycol (PEG) or the like. Otherwise, an anti-c-kit kinase antibody may be produced as a fusion protein with β-galactosidase, MBP (maltose binding protein), GST (glutathione S-transferase), GFP (green fluorescence protein) or the like, which can be detected in an ELISA method or the like without using a secondary antibody. An anti-c-kit kinase antibody may be modified by being labeled with biotin or the like such that the antibody can be collected using avidin, streptavidin or the like.

[0075] An anti-c-kit kinase antibody may be produced according to a conventional method using c-kit kinase or a partial fragment thereof (hereinafter, also referred to as a "polypeptide fragment of c-kit kinase"), or a cell expressing c-kit kinase or a partial fragment thereof as a sensitized antigen ("Current Protocols in Molecular Biology" (John Wiley & Sons (1987) Section 11.4-11.13)). In this case, a polypeptide fragment of c-kit kinase may be a fusion protein with an Fc region, GST, MBP, GFP, AP (alkaline phosphatase) or the like.

[0076] A polyclonal antibody and a monoclonal antibody may be prepared according to a method known by those skilled in the art (Antibodies: A Laboratory Manual, E. Harlow and D. Lane, ed., Cold Spring Harbor Laboratory (Cold Spring Harbor, NY, 1988)). A polyclonal antibody may be obtained, for example, by administering an antigen to a mammal such as a mouse, a rabbit or a rat, collecting blood from this mammal, and separating and purifying an antibody from the collected blood. Immune sensitization methods are known by those skilled in the art, and may be carried out, for example, by administering an antigen once or more. Furthermore, an antigen (a polypeptide fragment of c-kit kinase) may be used by dissolving it in an appropriate buffer such as a buffer containing a complete Freund's adjuvant or a generally used adjuvant such as aluminum hydroxide, although no adjuvant may be used depending on the administration route or conditions.

[0077] Blood is taken from the mammal 1-2 months after the last immune sensitization, and separated and purified according to a conventional method such as centrifugation, precipitation using ammonium sulfate or polyethyleneglycol and various chromatographies, thereby obtaining a polyclonal antibody as a polyclonal antiserum.

[0078] An example of a method for producing a monoclonal antibody includes a hybridoma technique. The hybridoma technique first sensitizes a mammal in the same manner as in the production of the polyclonal antibody. Preferably, partial blood collection is carried out appropriate days after the sensitization to determine the antibody titer by a known method such as ELISA method.

[0079] Subsequently, spleen is removed from the sensitized animal to obtain B cells. Then, the B cells are fused with myeloma cells by a common method to produce antibody-producing hybridomas. The myeloma cells used are not particularly limited and known cells may be used. The method for fusing the cells may be any method selected from methods known in the art such as Sendai virus technique, polyethyleneglycol technique and protoplast technique. The obtained hybridomas are cultured for an appropriate period of time in an HAT medium (a medium containing hypoxanthine, aminopterin and thymidine) by a common method for hybridoma selection. Then, the antibody-producing hybridoma of interest may be screened and cloned.

[0080] A known antibody detecting method such as ELISA method or radioimmunoassay method may be used as the screening method, and a method known in the art such as limiting dilution technique, FACS method or the like may be used as the cloning method. The obtained hybridoma may be cultured in an appropriate culture solution, or may be intraperitoneally administered, for example, to a mouse that is compatible with the hybridoma. The desired monoclonal antibody can be isolated and purified from the resulting culture solution or ascites by salt-out, ion-exchange chromatography, gel filtration, affinity chromatography or the like.

2. Pharmaceutical composition, kit and method for treating cancer

[0081] The present invention relates to a pharmaceutical composition, a kit, a method for treating cancer or the like characterized by combining a compound of the invention and a c-kit inhibitor.

[0082] According to the present invention, the c-kit inhibitor is not particularly limited as long as it has an activity of inhibiting c-kit kinase. Examples of the c-kit inhibitor include a c-kit kinase inhibitor and an anti-c-kit kinase antibody. Preferable examples of c-kit inhibitors include imatinib, SU5416, SU6668, SU11248, KRN633, PTK787/ZK222584, KRN951, AZD2171, AG013736, BAY 43-9006, AEE-788, PD180970, PD173955, MLN518 and BMS-354825, and more preferable example includes imatinib.

[0083] According to the present invention, the phrase "in combination" refers to a combination for combined use of the compound, and includes both a form for concomitantly using separate substances upon administration and a form as a mixture.

[0084] The dosage form of the formulation included in the kit of the invention is not particularly limited as long as it contains the compound of the invention and/or the c-kit inhibitor. The pharmaceutical composition and/or the kit of the invention is useful as a pharmaceutical composition and/or a kit for treating cancer.

[0085] The pharmaceutical composition and/or the kit of the invention may be used as a drug for treating cancer.

[0086] According to the present invention, a drug for treating cancer comprises an antitumor drug, a drug for improving prognosis of cancer, a drug for preventing cancer recurrence, a drug for suppressing cancer metastasis and the like.

[0087] The effect of cancer treatment may be confirmed by observation of a x-ray picture, CT or the like, by histopathological diagnosis of biopsy, or from a tumor marker value.

[0088] The pharmaceutical composition and/or the kit of the invention may be administered to a mammal (e.g., human, rat, rabbit, sheep, pig, bovine, cat, dog, monkey, etc.).

[0089] The types of cancer treated by the drug are not particularly limited.

[0090] The pharmaceutical composition and/or the kit of the invention may be used through oral or parental administration. When the pharmaceutical composition and/or the kit of the invention is used, the given dose of the compound of the invention differs depending on the degree of the symptom, age, sex, weight and sensitivity difference of the patient, administration mode, administration period, administration interval, nature, prescription and the type of the pharmaceutical formulation, and the type of the active element. Usually, but without limitation, the dose of the compound is 0.1-1000 mg/day, preferably 0.5-100 mg/day, more preferably 1-30 mg/day for an adult (weight 60 kg), which may be administered once to three times a day.

[0091] When the pharmaceutical composition and/or kit of the invention is used, the given dose of the c-kit inhibitor is usually, but without limitation, 10-6000 mg/day, preferably 50-4000 mg/day, more preferably 50-2000 mg/day for an adult, which may be administered once to three times a day.

[0092] In addition, when the pharmaceutical composition and/or the kit of the invention is used, the given dose of the c-kit kinase inhibitor is usually, but without limitation, 10-6000 mg/day, preferably 50-4000 mg/day, more preferably 50-2000 mg/day for an adult, which may be administered once to three times a day.

[0093] When the pharmaceutical composition and/or the kit of the invention is used, the given dose of an anti-c-kit kinase antibody is usually, but without limitation, 1-6000 mg/day, preferably 10-2000 mg/day, more preferably 10-1000 mg/day for an adult, which may be administered once a day or a week.

[0094] The amount of the compound of the invention used is not particularly limited and may differ according to the individual combination with the c-kit inhibitor, for example, it may be about 0.01-100 times (weight ratio) the amount of the c-kit inhibitor.

More preferably, it is about 0.1-10 times (weight ratio) the amount of the c-kit inhibitor.

[0095] The pharmaceutical composition of the invention may be made into various forms, for example, into solid oral formulations, injectable solution or the like.

[0096] Furthermore, each of the compound and the c-kit inhibitor contained in the kit of the invention may individually be made into solid oral formulations, injectable solution or the like.

[0097] In order to prepare a solid oral formulation, an excipient, and if necessary, a binder, disintegrant, lubricant, colorant, a flavoring agent and the like are added to the principal agent, and then made into a tablet, a coated tablet, granule, fine granule, dispersant, a capsule or the like according to a conventional method.

[0098] For example, lactose, cornstarch, sucrose, glucose, sorbit, crystalline cellulose, silicon dioxide or the like may be used as the excipient; for example, polyvinyl alcohol, ethyl cellulose, methyl cellulose, gum arabic, hydroxypropyl cellulose, hydroxypropylmethyl cellulose or the like may be used as the binder; for example, magnesium stearate, talc, silica or the like may be used as the lubricant; those that are allowed to be added to drugs may be used as the colorant; and for example, cocoa powder, menthol, aromatic acid, peppermint oil, camphor, cinnamon powder or the like may be used as the flavoring agent. Of course, if necessary, these tablets and granule may be coated appropriately with sugar coating, gelatin coating or else.

[0099] When an injectable solution is to be prepared, if necessary, the principal agent may be added with a pH adjuster, a buffer, a suspending agent, a solubilizing agent, a stabilizer, a tonicity agent, a preservative or the like, and may be made into an intravenously, subcutaneously or intramuscularly injectable solution according to a conventional method. If necessary, the solution may be made into a lyophilized form by a conventional technique.

[0100] Examples of the suspending agent include methyl cellulose, Polysorbate 80, hydroxyethyl cellulose, gum arabic, powdered tragacanth, carboxy methyl cellulose sodium and polyoxyethylene sorbitan monolaurate.

[0101] Examples of the solubilizing agent include polyoxyethylene hydrogenated castor oil, Polysorbate 80, nicotine acid amide, polyoxyethylene sorbitan monolaurate, macrogol, and castor oil fatty acid ethyl ester.

[0102] Examples of the stabilizer include sodium sulfite and sodium metasulfite; examples of the preservative include methyl parahydroxybenzoate, ethyl parahydroxybenzoate, sorbic acid, phenol, cresol and chlorocresol.

[0103] In the kit of the invention, a formulation containing the compound of the invention and a formulation containing the c-kit inhibitor may be mixed together or may be separately accommodated and packed together. The order of the formulations above is not particularly limited and they may be administered simultaneously or one may be administered after the other.

[0104] Besides the compound of the invention and the c-kit inhibitor, the pharmaceutical composition and/or the kit of the invention may also contain a package, an instruction, an attached document or the like. The package, the instruction, the attached document or the like may include description of a combination employed for using substances, and description of usage and dosage in the case of administering separate substances in combination or in the case of administering them in a form of a mixture. The usage and dosage may be described referring to the related description above.

[0105] The kit of the invention may also comprise: (a) at least one selected from the group consisting of a package, an instruction and an attached document describing combined use of the compound of the invention and the c-kit inhibitor; and (b) a pharmaceutical composition containing the compound of the invention. The kit is useful for treating cancer. The pharmaceutical composition containing the compound of the invention is useful for treating cancer. The package, the instruction, the attached document or the like may include the description of combined use of the compound, and description of usage and dosage in the case of administering separate substances in combination upon administration or in the case of administering them in the form of a mixture. The usage and dosage may be described referring to the description of pharmaceutical composition and kit above.

[0106] The present invention also comprises use of a compound of the invention for producing a pharmaceutical composition in combination with a c-kit inhibitor. According to the use of the invention, the pharmaceutical composition is useful for treating cancer.

[0107] The present invention also comprises a method for preventing or treating cancer comprising simultaneously or separately administering a compound of the invention and a c-kit inhibitor to a patient. According to the method of the invention for preventing or treating cancer, the route and the method for administering the compound of the invention and the c-kit inhibitor are not particularly limited and reference may be made to the description of the pharmaceutical composition of the invention above.

[0108] The present invention also comprises a pharmaceutical composition containing the compound of the invention which is simultaneously or separately administered with a c-kit inhibitor to a patient. For the pharmaceutical composition of the invention, the route and the method for administering the compound of the invention and the c-kit inhibitor are not particularly limited and reference may be made to the description of the pharmaceutical composition of the invention above.

EXAMPLES

[0109] Hereinafter, the present invention will be illustrated by way of specific examples, although the invention should not be limited thereto.

Example 1: Combinational use of compound of the invention and c-kit inhibitor in human cancer cell line subcutaneous xenograft model (*in vivo*)

[0110] Human gastrointestinal stromal tumor cell line GIST882 (supplied by The Brigham and Women's Hospital, Inc.) was cultured in RPMI1640 (containing 10% FBS) in a 5% carbon dioxide incubator to about 80% confluence. Following cultivation, each cell was collected by trypsin-EDTA treatment according to a general method. Using a phosphate buffer containing 50% matrigel, 5 x 10^7 cells/mL suspension was prepared, and 0.2 mL each of the resulting cell suspension was subcutaneously transplanted into the flank of a nude mouse. Starting from twenty-one days after the transplantation, 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide (10 mg/kg or 30 mg/kg, once a day, for two weeks) and imatinib (160 mg/kg, twice a day, for two weeks) were orally administered alone or in combination. 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide(methanesulfonate) was prepared based on the description of International publication No. 02/32872 pamphlet (WO02/32872). Moreover, imatinib was purchased from Novartis Pharma K.K. The major and minor axes of tumors were measured with Digimatic caliper (Mitsutoyo), and tumor volumes and relative tumor volumes were calculated according to the following formulae.

$$\text{Tumor Volume (TV)} = \text{Major axis of tumor (mm)} \times (\text{Minor axis of tumor})^2$$

$$(\text{mm}^2)/2$$

Relative Tumor Volume (RTV) = Tumor volume on measurement day/Tumor volume on the first administration day

[0111] As a result, combined use of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide and imatinib showed greater antitumor effect than the case where 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide or imatinib was used alone (Tables 1 and 2, Figures 1 and 2). Furthermore, combined use of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide and imatinib showed greater antitumor effect than the case where imatinib was used alone (Tables 1 and 2, Figures 1 and 2).

Table 1

Administered compound	Relative tumor volume on Day 15 Average ± standard deviation
Control (untreated)	2.71 ± 0.24
Imatinib 160 mg/kg	1.03 ± 0.15
Compound A 10 mg/kg	2.06 ± 0.16
Compound A 10 mg/kg + imatinib 160 mg/kg	0.77 ± 0.12

[0112] Table 1 shows antitumor effects obtained with 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide (indicated as Compound A in Table 1) alone, imatinib alone and combined use of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide and imatinib in human cancer cell line subcutaneous xenograft models. The first day of administration was considered Day 1.

Table 2

Administered compound	Relative tumor volume on Day 15 Average ± standard deviation
Control (untreated)	2.71±0.24
Imatinib 160 mg/kg	1.03±0.15
Compound A 30 mg/kg	1.36±0.13
Compound A 30 mg/kg + imatinib 160 mg/kg	0.62±0.09

[0113] Table 2 shows antitumor effects obtained with 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide (indicated as Compound A in Table 2) alone, imatinib alone and combined use of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide and imatinib in human cancer cell line subcutaneous xenograft models. The first day of administration was considered Day 1.

[0114] From the obtained results, the combination of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide and imatinib was found to provide a pharmaceutical composition and a kit that show a remarkable antitumor activity, which can be used for treating cancer.

[Reference Example]

[0115] Hereinafter, a method for producing a formulation of one of the compounds represented by Formula (I), 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide will be described as a reference example.

(Production of pharmaceutical composition)

(1) 1 mg tablet

[0116] 24g of crystal (C) of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide methanesulfonate (hereinafter, also referred to as "crystal (C)", which was produced according to the method described in Example 7 of WO2005/063713) and 192g of light anhydrous silicic acid (antigelling agent sold under the trade name of AEROSIL™200, Nippon Aerosil) were mixed with 20L Super Mixer, and then 1236g of D-mannitol (excipient, Towa-Kasei), 720g of crystalline cellulose (excipient sold under the trade name of Avicel PH101, Asahi Kasei) and 72g of hydroxypropylcellulose (binder sold under the trade name of HPC-L, Nippon Soda) were further added and mixed together. Subsequently, a suitable amount of anhydrous ethanol was added to obtain a granulated body containing crystal (C). This granulated body was dried in a rack dryer (60°C), and then size-regulated using PowerMILL to obtain granules. Together with the granules, 120g of croscarmellose sodium (disintegrant sold under the trade name of Ac-Di-Sol, FMC International Inc.) and 36g of sodium stearyl fumarate (lubricant, JRS Pharma LP) were placed in a 20L tumbler mixer and mixed together, and molded with a tablet machine to obtain tablets with a total mass of 100 mg per tablet. Moreover, the tablets were coated with a tablet coating machine using aqueous 10% Opadry yellow (OPADRY 03F42069 YELLOW, Colorcon Japan) solution as a coating solution, thereby obtaining coated tablets with a total mass of 105 mg per tablet.

(2) 10 mg tablet

[0117] 60g of crystal (C) and 192g of light anhydrous silicic acid (antigelling agent sold under the trade name of AEROSIL™200, Nippon Aerosil) were mixed with 20L Super Mixer, and then 1200g of D-mannitol (excipient, Towa-Kasei), 720g of crystalline cellulose (excipient sold under the trade name of Avicel PH101, Asahi Kasei) and 72g of hydroxypropylcellulose (binder sold under the trade name of HPC-L, Nippon Soda) were further added and mixed together. Subsequently, a suitable amount of anhydrous ethanol was added to obtain a granulated body containing crystal (C). This granulated body was dried in a rack dryer (60°C), and then size-regulated using PowerMILL to obtain granules. Together with the granules, 120g of croscarmellose sodium (disintegrant sold under the trade name of Ac-Di-Sol, FMC International Inc.) and 36g of sodium stearyl fumarate (lubricant, JRS Pharma LP) were placed in a 20L tumbler mixer and mixed together, and molded with a tablet machine to obtain tablets with a total mass of 400 mg per tablet. Moreover, the tablets were coated with a tablet coating machine using aqueous 10% Opadry yellow (OPADRY 03F42069 YELLOW, Colorcon Japan) solution as a coating solution, thereby obtaining coated tablets with a total mass of 411 mg per tablet.

(3) 100 mg tablet

[0118] 31.4g of crystal (C) and 4g of light anhydrous silicic acid (antigelling agent sold under the trade name of AEROSIL™200, Nippon Aerosil) were mixed with 1L Super Mixer, and then 40.1g of anhydrous calcium hydrogen phosphate (excipient, Kyowa Chemical Industry), 10g of low substituted hydroxypropylcellulose (binder sold under the trade name of L-HPC (LH-21), Shin-Etsu Chemical) and 3g of hydroxypropylcellulose (binder sold under the trade name of HPC-L, Nippon Soda) were further added and mixed together. Subsequently, a suitable amount of anhydrous ethanol was added to obtain a granulated body containing crystal (C). This granulated body was dried in a rack dryer (60°C), and then granulated using PowerMILL to obtain granules. Together with the granules, 10g of croscarmellose sodium (disintegrant sold under the trade name of Ac-Di-Sol, FMC International Inc.) and 1.5g of sodium stearyl fumarate (lubricant, JRS Pharma LP) were mixed and molded with a tablet machine to obtain tablets with a total mass of 400 mg per tablet.

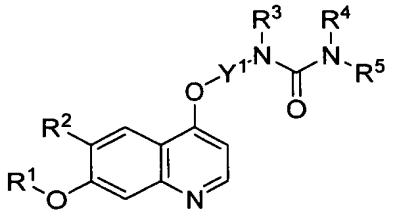
INDUSTRIAL APPLICABILITY

[0119] According to the present invention, there is provided a pharmaceutical composition and/or kit comprising a combination of a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof and a c-kit inhibitor, which can be used for treating cancer.

Claims

1. A pharmaceutical composition comprising a combination of a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof and a substance having a c-kit kinase-inhibiting activity:

Formula (I)

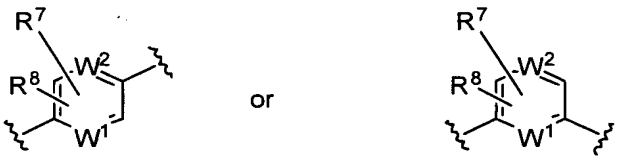


(I)

[wherein, R^1 represents group represented by Formula $-V^1-V^2-V^3$ (wherein, V^1 represents C_{1-6} alkylene group that may have a substituent; V^2 represents a single bond, an oxygen atom, a sulfur atom, carbonyl group, sulfinyl group, sulfonyl group, group represented by Formula $-CONR^6-$, group represented by Formula $-SO_2NR^6-$, group represented by Formula $-NR^6SO_2-$, group represented by Formula $-NR^6CO-$ or group represented by Formula $-NR^6-$ (wherein, R^6 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent or C_{3-8} cycloalkyl group that may have a substituent); V^3 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent);

R^2 represents cyano group, C_{1-6} alkoxy group that may have a substituent, carboxyl group, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula- $CONV^{a11}V^{a12}$ (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent);

Y^1 represents Formula



(wherein, R^7 and R^8 each independently represent a hydrogen atom, a halogen atom, cyano group, nitro group, amino group, C_{1-6} alkyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{1-6} alkoxy group that may have a substituent, C_{1-6} alkylthio group that may have a substituent, formyl group, C_{2-7} acyl group that may have a substituent, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{d1}V^{d2}$ (wherein, V^{d1} and V^{d2} each independently represent a hydrogen atom or C_{1-6} alkyl group that may have a substituent);

W^1 and W^2 each independently represent a carbon atom or a nitrogen atom that may have a substituent);

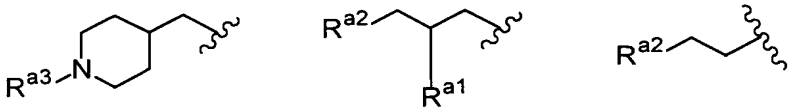
R^3 and R^4 each independently represent a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{2-7} acyl group that may have a substituent or C_{2-7} alkoxycarbonyl group that may have a substituent;

R^5 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have

a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent].

2. A pharmaceutical composition according to Claim 1, wherein R^1 is C_{1-6} alkyl group (where, R^1 may have a substituent selected from 3-10-membered nonaromatic heterocyclic group that may have C_{1-6} alkyl group, hydroxyl group, C_{1-6} alkoxy group, amino group, mono-C_{1-6} alkylamino group and di-C_{1-6} alkylamino group).

3. A pharmaceutical composition according to Claim 1, wherein R^1 is methyl group or group represented any one of the following Formulae:



(wherein, R^3 represents methyl group; R^{a1} represents a hydrogen atom or hydroxyl group; R^{a2} represents methoxy group, ethoxy group, 1-pyrrolidinyl group, 1-piperidinyl group, 4-morpholinyl group, dimethylamino group or diethylamino group).

4. A pharmaceutical composition according to Claim 1, wherein R^1 is methyl group or 2-methoxyethyl group.

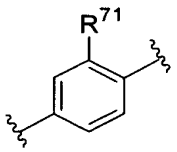
5. A pharmaceutical composition according to Claim 1, wherein R^2 represents cyano group or group represented by Formula $-CONV^{a11}V^{a12}$ (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent).

6. A pharmaceutical composition according to Claim 1, wherein R^2 is cyano group or group represented by Formula $-CONHV^{a16}$ (wherein, V^{a16} represents a hydrogen atom, C_{1-6} alkyl group, C_{3-8} cycloalkyl group, C_{1-6} alkoxy group or C_{3-8} cycloalkoxy group, where V^{a16} may have a substituent selected from a halogen atom, cyano group, hydroxyl group and C_{1-6} alkoxy group).

7. A pharmaceutical composition according to Claim 1, wherein R^2 is group represented by Formula $-CONHV^{a17}$ (wherein, V^{a17} represents a hydrogen atom, C_{1-6} alkyl group or C_{1-6} alkoxy group).

8. A pharmaceutical composition according to Claim 1, wherein R^2 is group represented by Formula $-CONHV^{a18}$ (wherein, V^{a18} represents a hydrogen atom, methyl group or methoxy group).

9. A pharmaceutical composition according to Claim 1, wherein Y^1 is group represented by Formula



(wherein, R^{71} represents a hydrogen atom or a halogen atom).

10. A pharmaceutical composition according to Claim 1, wherein R^3 and R^4 is a hydrogen atom.

11. A pharmaceutical composition according to Claim 1, wherein R^5 is a hydrogen atom, C_{1-6} alkyl group, C_{3-8} cycloalkyl group or C_{6-10} aryl group (where, R^5 may have a substituent selected from a halogen atom and methanesulfonyl group).

12. A pharmaceutical composition according to Claim 1, wherein R^5 is methyl group, ethyl group or cyclopropyl group.

13. A pharmaceutical composition according to Claim 1, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is at least one compound selected from the group consisting of:

N-(4-(6-cyano-7-(2-methoxyethoxy)-4-quinolyl)oxy-2-fluorophenyl)-N' -(4-fluorophenyl)urea;
N-(2-chloro-4-((6-cyano-7-((1-methyl-4-piperidyl)methoxy)-4-quinolyl)oxy)phenyl)-N'-cyclopropylurea;
N-(4-((6- cyano- 7-(((2R)- 3-(diethylamino)- 2- hydroxypropyl) oxy)- 4- quinolyl) oxy) phenyl)-N'-(4- fluorophenyl) urea;
N-(4-((6- cyano- 7-(((2R)- 2- hydroxy- 3-(1- pyrrolidino) propyl) oxy)- 4- quinolyl) oxy) phenyl)-N'-(4- fluorophenyl) urea;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N6-cyclopropyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-methoxyethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-fluoroethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6- methoxy- 4-(3- chloro- 4-(((cyclopropylamino) carbonyl) amino) phenoxy)- 7- methoxy- 6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-ethyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-hydroxyethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-((2S)-2,3-dihydroxypropyl)oxy-6-quinolinecarboxamide;
4-(3-chloro-4-(methylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methoxy-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-ethoxyethoxy)-6-quinolinecarboxamide;
4-(4-((cyclopropylamino)carbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N-(2-fluoro-4-((6-carbamoyl-7-methoxy-4-quinolyl)oxy)phenyl)-N'-cyclopropylurea;
N6-(2-hydroxyethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(1-propylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cis-2-fluoro-cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-(4-morpholino)ethoxy)-6--quinolinecarboxamide;
4-(3-chloro-4-(2-fluoroethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-((2R) tetrahydro-2-furanylmethyl)-4-(3- chloro-4-(((methylamino) carbonyl) amino) phenoxy)- 7- methoxy- 6-quinolinecarboxamide;
4-(3-fluoro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(((cyclopropylamino) carbonyl) amino) phenoxy)- 7-((2R)- 2- hydroxy- 3-(1- pyrrolidino) propoxy)- 6-quinolinecarboxamide;
N6- methyl- 4-(3- chloro- 4-(((methylamino) carbonyl) amino) phenoxy)- 7-((2R)- 3- diethylamino- 2- hydroxypropoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((2R)-3-diethylamino-2-hydroxypropoxy)-6-quinolinecarboxamide;
N6- methyl- 4-(3- chloro- 4-(((methylamino) carbonyl) amino) phenoxy)- 7-((2R)- 2- hydroxy- 3-(1- pyrrolidino) propoxy)-6-quinolinecarboxamide;

N6- methyl- 4-(3- chloro- 4-(((ethylamino) carbonyl) amino) phenoxy)- 7-((2R)- 2- hydroxy- 3-(1- pyrrolidino) propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-((1-methyl-4-piperidyl)methoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((1-methyl-4-piperidyl)methoxy)-6-quinolinecarboxamide;
N-(4-(6-cyano-7-(2-methoxyethoxy)-4-quinolyl)oxy-2-fluorophenyl)-N'-cyclopropylurea;
N-(4-(6-cyano-7-(3-(4-morpholino)propoxy)-4-quinolyl)oxyphenyl)-N'-(3-(methylsulfonyl)phenyl)urea;
4-(4-((cyclopropylamino)carbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-((2-fluoroethylamino)carbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-ethoxyethyl)-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(4-(3-ethylureido)-3-fluoro-phenoxy)-7-methoxyquinoline-6-carboxylic acid (2-cyanoethyl)amide; and
N-(4-(6-(2-cyanoethyl)carbamoyl-7-methoxy-4-quinolyl)oxy-2-fluorophenyl)-N'-cyclopropylurea,

a pharmacologically acceptable salt thereof or a solvate thereof.

14. A pharmaceutical composition according to Claim 1, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is at least one compound selected from the group consisting of:

4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6- methoxy-4-(3- chloro-4-(((cyclopropylamino) carbonyl) amino) phenoxy)- 7- methoxy- 6-quinolinecarboxamide;
4-(3-chloro-4-(methylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide; and
N6-methoxy-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide,

a pharmacologically acceptable salt thereof or a solvate thereof.

15. A pharmaceutical composition according to Claim 1, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof, or a solvate thereof is 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide, a pharmacologically acceptable salt thereof, or a solvate thereof.

16. A pharmaceutical composition according to Claim 1, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof, or a solvate thereof is methanesulfonate of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide.

17. A pharmaceutical composition according to any one of Claims 1-16, wherein the substance having a c-kit kinase-inhibiting activity is at least one compound selected from the group consisting of:

(1) 4-(4-methylpiperazine-1-ylmethyl)-N-[4-methyl-3-[4-(3-pyridyl)pyrimidine-2-ylamino]phenyl]benzenamide;
(2) 3-[(2,4-dimethylpyrrole-5-yl)methylene]-2-indolinone;
(3) (Z)-3-[(2,4-dimethyl-5-(2-oxo-1,2-dihydroindole-3-ylidenemethyl)-1H-pyrrole-3-yl)-propionic acid;
(4) 5-(5-fluoro-2-oxo-1,2-dihydroindole-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide;
(5) N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-propylurea;
(6) 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine;
(7) N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea;
(8) 4-[(4-fluoro-2-methylindole-5-yl)oxy]-6-methoxy-7-[3-(pyrrolidine-1-yl)propoxy]quinazoline;
(9) 6-[2-(methylcarbamoyl)phenylsulfanil]-3-E-[2-(pyridine-2-yl)ethenyl]indazole;
(10) N-(3-trifluoromethyl-4-chlorophenyl)-N'-(4-(2-methylcarbamoylpyridine-4-yl)oxyphenyl)urea;
(11) [6-[4-[(4-ethylpiperazine-1-yl)methyl]phenyl]-7H-pyrrolo[2,3-d]pyrimidine-4-yl]-((R)-1-phenylethyl)amine;
(12) 6-(2,6-dichloro-phenyl)-2-(4-fluoro-3-methyl-phenylamino)-8-methyl8H-pyrido[2,3-d]pyrimidine-7-one;
(13) 6-(2,6-dichlorophenyl)-8-methyl-2-(3-methylsulfanilphenylamino)-8H-pyrido [2,3-/d/]pyrimidine-7-one;
(14) 4-[6-methoxy-7-(3-piperidine-1-yl-propoxy)quinazoline-4-yl]piperazine-1-carboxylic acid(4-isopropoxyphenyl)amide; and
(15) N-(2-chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)piperazine-1-yl]-2-methylpyrimidine-4-yl]amino]thiazole-5-carboxamide,

a pharmacologically acceptable salt thereof or a solvate thereof.

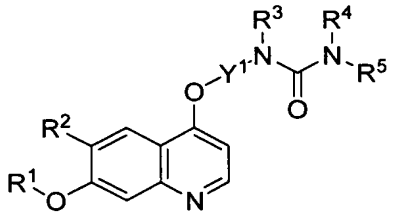
18. A pharmaceutical composition according to any one of Claims 1-16, wherein the substance having a c-kit kinase-inhibiting activity is 4-(4-methylpiperazine-1-ylmethyl)-N-[4-methyl-3-[4-(3-pyridyl)pyrimidine-2-ylamino]phenyl]benzenamide, a pharmacologically acceptable salt thereof, or a solvate thereof.

19. A pharmaceutical composition according to any one of Claims 1-16, wherein the substance having a c-kit kinase-inhibiting activity is an anti-c-kit kinase antibody.

20. A pharmaceutical composition according to any one of Claims 1-19, wherein a pharmaceutical composition is a pharmaceutical composition for cancer treatment.

21. A kit comprising: (a) at least one selected from the group consisting of a package, an instruction and an attached document describing combined use of a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof with a substance having a c-kit kinase-inhibiting activity; and (b) a pharmaceutical composition comprising a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof:

Formula (I)

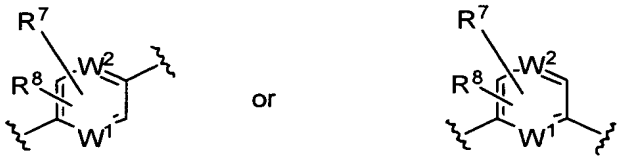


(I)

[wherein, R^1 represents group represented by Formula $-V^1-V^2-V^3$ (wherein, V^1 represents C_{1-6} alkylene group that may have a substituent; V^2 represents a single bond, an oxygen atom, a sulfur atom, carbonyl group, sulfinyl group, sulfonyl group, group represented by Formula $-CONR^6-$, group represented by Formula $-SO_2NR^6-$, group represented by Formula $-NR^6SO_2-$, group represented by Formula $-NR^6CO-$ or group represented by Formula $-NR^6-$ (wherein, R^6 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent or C_{3-8} cycloalkyl group that may have a substituent); V^3 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent);

R^2 represents cyano group, C_{1-6} alkoxy group that may have a substituent, carboxyl group, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{a11}V^{a12}$ (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent);

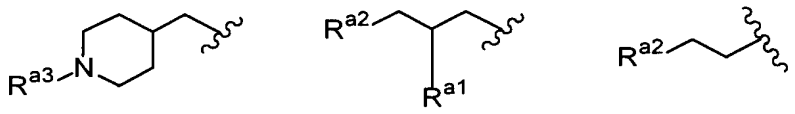
Y^1 represents group represented by Formula



(wherein, R^7 and R^8 each independently represent a hydrogen atom, a halogen atom, cyano group, nitro group, amino group, C_{1-6} alkyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{1-6} alkoxy group that may have a substituent, C_{1-6} alkylthio group that may have a substituent, formyl group, C_{2-7} acyl group that may have a substituent, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{d1}V^{d2}$ (wherein, V^{d1} and V^{d2} each independently represent a hydrogen atom or C_{1-6} alkyl group that may have a substituent);
W^1 and W^2 each independently represent a carbon atom or a nitrogen atom that may have a substituent);
R^3 and R^4 each independently represent a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{2-7} acyl group that may have a substituent or C_{2-7} alkoxycarbonyl group that may have a substituent;
R^5 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent].

22. A kit according to Claim 21, wherein R^1 is C_{1-6} alkyl group (where, R^1 may have a substituent selected from 3-10-membered nonaromatic heterocyclic group that may have C_{1-6} alkyl group, hydroxyl group, C_{1-6} alkoxy group, amino group, mono-C_{1-6} alkylamino group and di-C_{1-6} alkylamino group).

23. A kit according to Claim 21, wherein R^1 is methyl group or group represented by any one of the following Formulae



(wherein, R^{a3} represents methyl group; R^{a1} represents a hydrogen atom or hydroxyl group; R^{a2} represents methoxy group, ethoxy group, 1-pyrrolidinyl group, 1-piperidinyl group, 4-morpholinyl group, dimethylamino group or diethylamino group).

24. A kit according to Claim 21, wherein R^1 is methyl group or 2-methoxyethyl group.

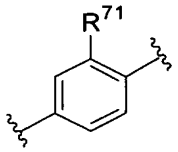
25. A kit according to Claim 21, wherein R^2 is cyano group or group represented by Formula $-CONV^{a11}V^{a12}$ (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent).

26. A kit according to Claim 21, wherein R^2 is cyano group or group represented by Formula $-CONHV^{a16}$ (wherein, V^{a16} represents a hydrogen atom, C_{1-6} alkyl group, C_{3-8} cycloalkyl group, C_{1-6} alkoxy group or C_{3-8} cycloalkoxy group, where V^{a16} may have a substituent selected from a halogen atom, cyano group, hydroxyl group and C_{1-6} alkoxy group).

27. A kit according to Claim 21, wherein R^2 is group represented by Formula -CONHV^{a17} (wherein, V^{a17} represents a hydrogen atom, C_{1-6} alkyl group or C_{1-6} alkoxy group).

28. A kit according to Claim 21, wherein R^2 is group represented by Formula -CONHV^{a18} (wherein, V^{a18} represents a hydrogen atom, methyl group or methoxy group).

29. A kit according to Claim 21, wherein Y^1 is group represented by Formula



(wherein, R^{71} represents a hydrogen atom or a halogen atom).

30. A kit according to Claim 21, wherein R^3 and R^4 are hydrogen atoms.

31. A kit according to Claim 21, wherein R^5 is a hydrogen atom, C_{1-6} alkyl group, C_{3-8} cycloalkyl group or C_{6-10} aryl group (where, R^5 may have a substituent selected from a halogen atom and methanesulfonyl group).

32. A kit according to Claim 21, wherein R^5 is methyl group, ethyl group or cyclopropyl group.

33. A kit according to Claim 21, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is at least one compound selected from the group consisting of:

N-(4-(6-cyano-7-(2-methoxyethoxy)-4-quinolyl)oxy-2-fluorophenyl)-N'-(4-fluorophenyl)urea;
N-(2-chloro-4-((6-cyano-7-((1-methyl-4-piperidyl)methoxy)-4-quinolyl)oxy)phenyl)-N'-cyclopropylurea;
N-(4-((6-cyano-7-(((2R)-3-(diethylamino)-2-hydroxypropyl)oxy)-4-quinolyl)oxy)phenyl)-N'-(4-fluorophenyl)urea;
N-(4-((6-cyano-7-(((2R)-2-hydroxy-3-(-pyrrolidino)propyl)oxy)-4-quinolyl)oxy)phenyl)-N'-(4-fluorophenyl)urea;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N6-cyclopropyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-methoxyethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-fluoroethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methoxy-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-ethyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-hydroxyethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-((2S)-2,3-dihydroxypropyl)oxy-6-quinolinecarboxamide;
4-(3-chloro-4-(methylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methoxy-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-ethoxyethoxy)-6-quinolinecarboxamide;
4-(4-((cyclopropylamino)carbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N-(2-fluoro-4-((6-carbamoyl-7-methoxy-4-quinolyl)oxy)phenyl)-N'-cyclopropylurea;
N6-(2-hydroxyethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(1-propylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;

4-(3-chloro-4-(cis-2-fluoro-cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl) aminophenoxy)-7-(2-(4-morpholino) ethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(2-fluoroethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-((2R) tetrahydro-2-furanylmethyl)-4-(3-chloro-4-(((methylamino) carbonyl) amino) phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(((cyclopropylamino) carbonyl) amino) phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino) propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino) carbonyl) amino) phenoxy)-7-((2R)-3-diethylamino-2-hydroxypropoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((2R)-3-diethylamino-2-hydroxypropoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino) carbonyl) amino) phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino) propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino) carbonyl) amino) phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino) propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-((1-methyl-4-piperidyl)methoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((1-methyl-4-piperidyl)methoxy)-6-quinolinecarboxamide;
N-(4-(6-cyano-7-(2-methoxyethoxy)-4-quinolyl)oxy-2-fluorophenyl)-N'-cyclopropylurea;
N-(4-(6-cyano-7-(3-(4-morpholino)propoxy)-4-quinolyl)oxyphenyl)-N'-(3-(methylsulfonyl)phenyl)urea;
4-(4-((cyclopropylamino)carbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-((2-fluoroethylamino)carbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-ethoxyethyl)-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(4-(3-ethylureido)-3-fluoro-phenoxy)-7-methoxyquinoline-6-carboxylic acid (2-cyanoethyl)amide; and
N-(4-(6-(2-cyanoethyl)carbamoyl-7-methoxy-4-quinolyl)oxy-2-fluorophenyl)-N'-cyclopropylurea,

a pharmacologically acceptable salt thereof, or a solvate thereof.

34. A kit according to Claim 21, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is at least one compound selected from the group consisting of:

4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide,
N6-methoxy-4-(3-chloro-4-(((cyclopropylamino) carbonyl) amino) phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(methylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide; and
N6-methoxy-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide,

a pharmacologically acceptable salt thereof, or a solvate thereof.

35. A kit according to Claim 21, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide, a pharmacologically acceptable salt thereof or a solvate thereof.

36. A kit according to Claim 21, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is methanesulfonate of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide.

37. A kit according to any one of Claims 21-36, wherein the substance having a c-kit kinase-inhibiting activity is at least one compound selected from the group consisting of:

(1) 4-(4-methylpiperazine-1-ylmethyl)-N-[4-methyl-3-[4-(3-pyridyl)pyrimidine-2-ylamino]phenyl]benzenamide;
(2) 3-[(2,4-dimethylpyrrole-5-yl)methylene]-2-indolinone;
(3) (Z)-3-[(2,4-dimethyl-5-(2-oxo-1,2-dihydroindole-3-ylidenemethyl)-1H-pyrrole-3-yl)-propionic acid;
(4) 5-(5-fluoro-2-oxo-1,2-dihydroindole-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide;
(5) N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-propylurea;
(6) 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine;
(7) N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea;
(8) 4-[(4-fluoro-2-methylindole-5-yl)oxy]-6-methoxy-7-[3-(pyrrolidine-1-yl)propoxy]quinazoline;
(9) 6-[2-(methylcarbamoyl)phenylsulfanil]-3-E-[2-(pyridine-2-yl)ethenyl]indazole;
(10) N-(3-trifluoromethyl-4-chlorophenyl)-N'-(4-(2-methylcarbamoylpyridine-4-yl)oxyphenyl)urea;
(11) [6-[4-[(4-ethylpiperazine-1-yl)methyl]phenyl]-7H-pyrrolo[2,3-d]pyrimidine-4-yl]-((R)-1-phenylethyl)amine;
(12) 6-(2,6-dichloro-phenyl)-2-(4-fluoro-3-methyl-phenylamino)-8-methyl8H-pyrido[2,3-d]pyrimidine-7-one;
(13) 6-(2,6-dichlorophenyl)-8-methyl-2-(3-methylsulfanilphenylamino)-8H-pyrido[2,3-/d/]pyrimidine-7-one;
(14) 4-[6-methoxy-7-(3-piperidine-1-yl-propoxy)quinazoline-4-yl]piperazine-1-carboxylic acid(4-isopropoxyphenyl)amide; and
(15)N-(2-chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)piperazine-1-yl]-2-methylpyrimidine-4-yl]amino]thiazole-5-carboxamide,

a pharmacologically acceptable salt thereof, or a solvate thereof.

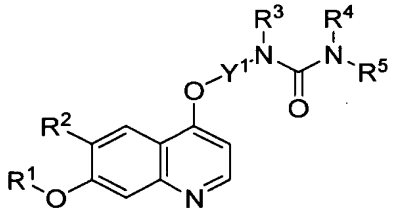
38. A kit according to any one of Claims 21-36, wherein the substance having a c-kit kinase-inhibiting activity is 4-(4-methylpiperazine-1-ylmethyl)-N-[4-methyl-3-[4-(3-pyridyl)pyrimidine-2-ylamino]phenyl]benzenamide, a pharmacologically acceptable salt thereof or a solvate thereof.

39. A kit according to any one of Claims 21-36, wherein the substance having a c-kit kinase-inhibiting activity is an anti-c-kit kinase antibody.

40. A kit according to any one of Claims 21-39, which is a kit for cancer treatment.

41. A kit comprising a set of a formulation containing the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof, and a formulation containing a substance having a c-kit kinase-inhibiting activity:

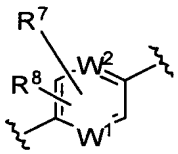
Formula (I)

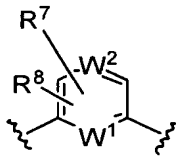


(I)

[wherein, R^1 represents group represented by Formula $-V^1-V^2-V^3$ (wherein, V^1 represents C_{1-6} alkylene group that may have a substituent; V^2 represents a single bond, an oxygen atom, a sulfur atom, carbonyl group, sulfinyl group, sulfonyl group, group represented by Formula $-CONR^6-$, group represented by Formula $-SO_2NR^6-$, group represented by Formula $-NR^6SO_2-$, group represented by Formula $-NR^6CO-$ or group represented by Formula $-NR^6-$ (wherein, R^6 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent or C_{3-8} cycloalkyl group that may have a substituent); V^3 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent);
R^2 represents cyano group, C_{1-6} alkoxy group that may have a substituent, carboxyl group, C_{2-7} alkoxycarbonyl

group that may have a substituent or group represented by Formula -CONV^{a11}V^{a12} (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent);
Y^1 represents group represented by Formula

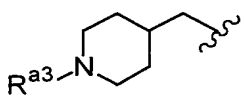


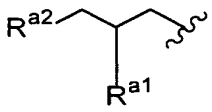
or


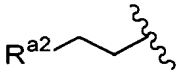
(wherein, R^7 and R^8 each independently represent a hydrogen atom, a halogen atom, cyano group, nitro group, amino group, C_{1-6} alkyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{1-6} alkoxy group that may have a substituent, C_{1-6} alkylthio group that may have a substituent, formyl group, C_{2-7} acyl group that may have a substituent, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula -CONV^{d1}V^{d2} (wherein, V^{d1} and V^{d2} each independently represent a hydrogen atom or C_{1-6} alkyl group that may have a substituent);
W^1 and W^2 each independently represent a carbon atom or a nitrogen atom that may have a substituent);
R^3 and R^4 each independently represent a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{2-7} acyl group that may have a substituent or C_{2-7} alkoxycarbonyl group that may have a substituent;
R^5 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent].

42. A kit according to Claim 41, wherein R^1 is C_{1-6} alkyl group (where, R^1 may have a substituent selected from 3-10-membered nonaromatic heterocyclic group that may have C_{1-6} alkyl group, hydroxyl group, C_{1-6} alkoxy group, amino group, mono-C_{1-6} alkylamino group and di-C_{1-6} alkylamino group).

43. A kit according to Claim 41, wherein R^1 is methyl group or group represented by any of the following Formulae







(wherein, R^{a3} represents methyl group; R^{a1} represents a hydrogen atom or hydroxyl group; R^{a2} represents methoxy group, ethoxy group, 1-pyrrolidinyl group, 1-piperidinyl group, 4-morpholinyl group, dimethylamino group or diethylamino group).

44. A kit according to Claim 41, wherein R^1 is methyl group or 2-methoxyethyl group.

45. A kit according to Claim 41, wherein R^2 is cyano group or group represented by Formula -CONV^{a11}V^{a12} (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-

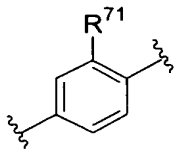
membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent).

46. A kit according to Claim 41, wherein R^2 represents cyano group or group represented by Formula -CONHV^{a16} (wherein, V^{a16} represents a hydrogen atom, C_{1-6} alkyl group, C_{3-8} cycloalkyl group, C_{1-6} alkoxy group or C_{3-8} cycloalkoxy group, where V^{a16} may have a substituent selected from a halogen atom, cyano group, hydroxyl group and C_{1-6} alkoxy group).

47. A kit according to Claim 41, wherein R^2 is group represented by Formula -CONHV^{a17} (wherein, V^{a17} represents a hydrogen atom, C_{1-6} alkyl group or C_{1-6} alkoxy group).

48. A kit according to Claim 41, wherein R^2 is group represented by Formula -CONHV^{a18} (wherein, V^{a18} represents a hydrogen atom, methyl group or methoxy group).

49. A kit according to Claim 41, wherein Y^1 is group represented by Formula



(wherein, R^{71} represents a hydrogen atom or a halogen atom).

50. A kit according to Claim 41, wherein R^3 and R^4 are hydrogen atoms.

51. A kit according to Claim 41, wherein R^5 is a hydrogen atom, C_{1-6} alkyl group, C_{3-8} cycloalkyl group or C_{6-10} aryl group (where R^5 may have a substituent selected from a halogen atom and methanesulfonyl group).

52. A kit according to Claim 41, wherein R^5 is methyl group, ethyl group or cyclopropyl group.

53. A kit according to Claim 41, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is at least one compound selected from the group consisting of:

N-(4-(6-cyano-7-(2-methoxyethoxy)-4-quinolyl)oxy-2-fluorophenyl)-N'-(4-fluorophenyl)urea;
N-(2-chloro-4-((6-cyano-7-((1-methyl-4-piperidyl)methoxy)-4-quinolyl)oxy)phenyl)-N'-cyclopropylurea;
N-(4-((6-cyano-7-(((2R)-3-(diethylamino)-2-hydroxypropyl)oxy)-4-quinolyl)oxy)phenyl)-N'-(4-fluorophenyl)urea;
N-(4-((6-cyano-7-(((2R)-2-hydroxy-3-(1-pyrrolidino)propyl)oxy)-4-quinolyl)oxy)phenyl)-N'-(4-fluorophenyl)urea;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N6-cyclopropyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-methoxyethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-fluoroethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methoxy-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;

N6-ethyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-hydroxyethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-((2S)-2,3-dihydroxypropyl)oxy-6-quinolinecarboxamide;
4-(3-chloro-4-(methylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methoxy-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-ethoxyethoxy)-6-quinolinecarboxamide;
4-(4-((cyclopropylamino)carbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N-(2-fluoro-4-((6-carbamoyl-7-methoxy-4-quinolyl)oxy)phenyl)-N'-cyclopropylurea;
N6-(2-hydroxyethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(1-propylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cis-2-fluoro-cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-(4-morpholino)ethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(2-fluoroethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-((2R)tetrahydro-2-furanylmethyl)-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino)propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-((2R)-3-diethylamino-2-hydroxypropoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((2R)-3-diethylamino-2-hydroxypropoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino)propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino)propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-((1-methyl-4-piperidyl)methoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((1-methyl-4-piperidyl)methoxy)-6-quinolinecarboxamide;
N-(4-(6-cyano-7-(2-methoxyethoxy)-4-quinolyl)oxy-2-fluorophenyl)-N'-cyclopropylurea;
N-(4-(6-cyano-7-(3-(4-morpholino)propoxy)-4-quinolyl)oxyphenyl)-N'-(3-(methylsulfonyl)phenyl)urea;
4-(4-((cyclopropylamino)carbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-((2-fluoroethylamino)carbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-ethoxyethyl)-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(4-(3-ethylureido)-3-fluoro-phenoxy)-7-methoxyquinoline-6-carboxylic acid (2-cyanoethyl)amide; and
N-(4-(6-(2-cyanoethyl)carbamoyl-7-methoxy-4-quinolyl)oxy-2-fluorophenyl)-N'-cyclopropylurea,

a pharmacologically acceptable salt thereof, or a solvate thereof.

54. A kit according to Claim 41, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is at least one compound selected from the group consisting of:

4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methoxy-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(methylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide; and
N6-methoxy-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide,

a pharmacologically acceptable salt thereof, or a solvate thereof.

55. A kit according to Claim 41, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide, a pharmacologically acceptable salt thereof, or a solvate thereof.

56. A kit according to Claim 41, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is methanesulfonate of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide.

57. A kit according to any one of Claims 41-56, wherein the substance having a c-kit kinase-inhibiting activity is at least one compound selected from the group consisting of:

(1) 4-(4-methylpiperazine-1-ylmethyl)-N-[4-methyl-3-[4-(3-pyridyl)pyrimidine-2-ylamino]phenyl]benzenamide;
(2) 3-[(2,4-dimethylpyrrole-5-yl)methylene]-2-indolinone;
(3) (Z)-3-[(2,4-dimethyl-5-(2-oxo-1,2-dihydroindole-3-ylidenemethyl)-1H-pyrrole-3-yl)-propionic acid;
(4) 5-(5-fluoro-2-oxo-l,2-dihydroindole-3-ylidenemethyl)-2,4-dimethyl-lH-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide;
(5) N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-propylurea,
(6) 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine;
(7) N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}-N'-(5-methyl-3-isoxazolyl)urea;
(8) 4-[(4-fluoro-2-methylindole-5-yl)oxy]-6-methoxy-7-[3-(pyrrolidine-1-yl)propoxy]quinazoline;
(9) 6-[2-(methylcarbamoyl)phenylsulfanil]-3-E-[2-(pyridine-2-yl)ethenyl]indazole;
(10) N-(3-trifluoromethyl-4-chlorophenyl)-N'-(4-(2-methylcarbamoylpyridine-4-yl)oxyphenyl)urea;
(11) [6-[4-[(4-ethylpiperazine-1-yl)methyl]phenyl]-7H-pyrrolo[2,3-d]pyrimidine-4-yl]-((R)-1-phenylethyl)amine;
(12) 6-(2,6-dichloro-phenyl)-2-(4-fluoro-3-methyl-phenylamino)-8-methyl8H-pyrido[2,3-d]pyrimidine-7-one;
(13) 6-(2,6-dichlorophenyl)-8-methyl-2-(3-methylsulfanilphenylamino)-8H-pyrido[2,3-/d/]pyrimidine-7-one;
(14) 4-[6-methoxy-7-(3-piperidine-1-yl-propoxy)quinazoline-4-yl]piperazine-1-carboxylic acid(4-isopropoxyphenyl)amide; and
(15) N-(2-chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)piperazine-1-yl]-2-methylpyrimidine-4-yl]amino]thiazole-5-carboxamide,

a pharmacologically acceptable salt thereof, or a solvate thereof.

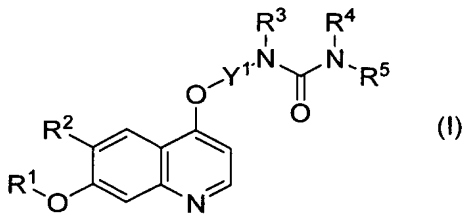
58. A kit according to any one of Claims 41-56, wherein the substance having a c-kit kinase-inhibiting activity is 4-(4-methylpiperazine-1-ylmethyl)-N-[4-methyl-3-[4-(3-pyridyl)pyrimidine-2-ylamino]phenyl]benzenamide, a pharmacologically acceptable salt thereof or a solvate thereof.

59. A kit according to any one of Claims 41-56, wherein the substance having a c-kit kinase-inhibiting activity is an anti-c-kit kinase antibody.

60. A kit according to any one of Claims 41-59, wherein the kit is for cancer treatment.

61. A pharmaceutical composition comprising a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof, which is administered simultaneously or separately to a patient with a substance having a c-kit kinase-inhibiting activity:

Formula (I)

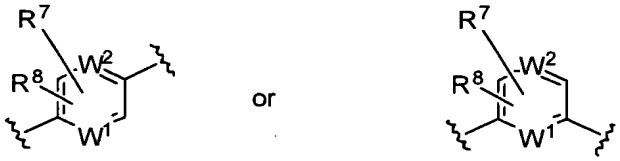


(I)

[wherein, R^1 represents group represented by Formula $-V^1-V^2-V^3$ (wherein, V^1 represents C_{1-6} alkylene group that may have a substituent; V^2 represents a single bond, an oxygen atom, a sulfur atom, carbonyl group, sulfinyl group, sulfonyl group, group represented by Formula $-CONR^6-$, group represented by Formula $-SO_2NR^6-$, group represented by Formula $-NR^6SO_2-$, group represented by Formula $-NR^6CO-$ or group represented by Formula $-NR^6-$ (wherein, R^6 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent or C_{3-8} cycloalkyl group that may have a substituent); V^3 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent);

R^2 represents cyano group, C_{1-6} alkoxy group that may have a substituent, carboxyl group, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{a11}V^{a12}$ (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent);

Y^1 represents group represented by Formula



(wherein, R^7 and R^8 each independently represent a hydrogen atom, a halogen atom, cyano group, nitro group, amino group, C_{1-6} alkyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{1-6} alkoxy group that may have a substituent, C_{1-6} alkylthio group that may have a substituent, formyl group, C_{2-7} acyl group that may have a substituent, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{d1}V^{d2}$ (wherein, V^{d1} and V^{d2} each independently represent a hydrogen atom or C_{1-6} alkyl group that may have a substituent);

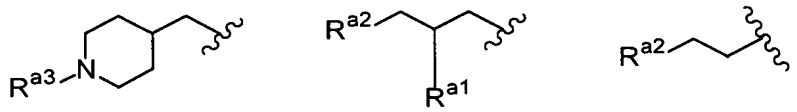
W^1 and W^2 each independently represent a carbon atom or a nitrogen atom that may have a substituent);

R^3 and R^4 each independently represent a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{2-7} acyl group that may have a substituent or C_{2-7} alkoxycarbonyl group that may have a substituent;

R^5 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent].

62. A pharmaceutical composition according to Claim 61, wherein R^1 is C_{1-6} alkyl group (where R^1 may have a substituent selected from 3-10-membered nonaromatic heterocyclic group that may have C_{1-6} alkyl group, hydroxyl group, C_{1-6} alkoxy group, amino group, mono-C_{1-6} alkylamino group and di-C_{1-6} alkylamino group).

63. A pharmaceutical composition according to Claim 61, wherein R^1 is methyl group or group represented by any one of the following Formulae



(wherein, R^{a3} represents methyl group; R^{a1} represents a hydroxyl group; R^{a2} represents methoxy group, ethoxy group, 1-pyrrolidinyl group, 1-piperidinyl group, 4-morpholinyl group, dimethylamino group or diethylamino group).

64. A pharmaceutical composition according to Claim 61, wherein R^1 is methyl group or 2-methoxyethyl group.

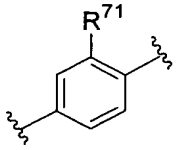
65. A pharmaceutical composition according to Claim 61, wherein R^2 is cyano group or group represented by Formula $-CONV^{a11}V^{a12}$ (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent).

66. A pharmaceutical composition according to Claim 61, wherein R^2 represents cyano group or group represented by Formula $-CONHV^{a16}$ (wherein, V^{a16} represents a hydrogen atom, C_{1-6} alkyl group, C_{3-8} cycloalkyl group, C_{1-6} alkoxy group or C_{3-8} cycloalkoxy group, where V^{a16} may have a substituent selected from a halogen atom, cyano group, hydroxyl group and C_{1-6} alkoxy group).

67. A pharmaceutical composition according to Claim 61, wherein R^2 is group represented by Formula $-CONHV^{a17}$ (wherein, V^{a17} represents a hydrogen atom, C_{1-6} alkyl group or C_{1-6} alkoxy group).

68. A pharmaceutical composition according to Claim 61, wherein R^2 is group represented by Formula $-CONHV^{a18}$ (wherein, V^{a18} represents a hydrogen atom, methyl group or methoxy group).

69. A pharmaceutical composition according to Claim 61, wherein Y^1 is group represented by Formula



(wherein, R^{71} represents a hydrogen atom or a halogen atom).

70. A pharmaceutical composition according to Claim 61, wherein R^3 and R^4 are hydrogen atoms.

71. A pharmaceutical composition according to Claim 61, wherein R^5 is a hydrogen atom, C_{1-6} alkyl group, C_{3-8} cycloalkyl group or C_{6-10} aryl group (where, R^5 may have a substituent selected from a halogen atom and methanesulfonyl group).

72. A pharmaceutical composition according to Claim 61, wherein R^5 is methyl group, ethyl group or cyclopropyl group.

73. A pharmaceutical composition according to Claim 61, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is at least one compound selected from the group consisting of

N-(4-(6-cyano-7-(2-methoxyethoxy)-4-quinolyl)oxy-2-fluorophenyl)-N'-(4-fluorophenyl)urea;
N-(2-chloro-4-((6-cyano-7-((1-methyl-4-piperidyl)methoxy)-4-quinolyl)oxy)phenyl)-N'-cyclopropylurea;
N-(4-((6-cyano-7-(((2R)-3-(diethylamino)-2-hydroxypropyl)oxy)-4-quinolyl)oxy)phenyl)-N'-(4-fluorophenyl)urea;
N-(4-((6-cyano-7-(((2R)-2-hydroxy-3-(1-pyrrolidino)propyl)oxy)-4-quinolyl)oxy)phenyl)-N'-(4-fluorophenyl)urea;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N6-cyclopropyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-methoxyethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-fluoroethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methoxy-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-ethyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-hydroxyethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-((2S)-2,3-dihydroxypropyl)oxy-6-quinolinecarboxamide;
4-(3-chloro-4-(methylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide,
N6-methoxy-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-ethoxyethoxy)-6-quinolinecarboxamide;
4-(4-((cyclopropylamino)carbonyl)aminophenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N-(2-fluoro-4-((6-carbamoyl-7-methoxy-4-quinolyl)oxy)phenyl)-N'-cyclopropylurea;
N6-(2-hydroxyethyl)-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(1-propylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cis-2-fluoro-cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-(2-methoxyethoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-(2-(4-morpholino)ethoxy)-6-quinolinecarboxamide;
4-(3-chloro-4-(2-fluoroethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-((2R)tetrahydro-2-furanylmethyl)-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-fluoro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino)propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-((2R)-3-diethylamino-2-hydroxypropoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((2R)-3-diethylamino-2-hydroxypropoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino)propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((2R)-2-hydroxy-3-(1-pyrrolidino)propoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-((1-methyl-4-piperidyl)methoxy)-6-quinolinecarboxamide;
N6-methyl-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-((1-methyl-4-piperidyl)methoxy)-6-quinolinecarboxamide;
N-(4-(6-cyano-7-(2-methoxyethoxy)-4-quinolyl)oxy-2-fluorophenyl)-N'-cyclopropylurea;
N-(4-(6-cyano-7-(3-(4-morpholino)propoxy)-4-quinolyl)oxyphenyl)-N'-(3-(methylsulfonyl)phenyl)urea;
4-(4-((cyclopropylamino)carbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;

4-(3-fluoro-4-((2-fluoroethylamino)carbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-(2-ethoxyethyl)-4-(3-chloro-4-(((methylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(4-(3-ethylureido)-3-fluoro-phenoxy)-7-methoxyquinoline-6-carboxylic acid (2-cyanoethyl)amide; and
N-(4-(6-(2-cyanoethyl)carbamoyl-7-methoxy-4-quinolyl)oxy-2-fluorophenyl)-N'-cyclopropylurea,

a pharmacologically acceptable salt thereof or a solvate thereof.

74. A pharmaceutical composition according to Claim 61, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is at least one compound selected from the group consisting of:

4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(ethylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide;
N6-methoxy-4-(3-chloro-4-(((cyclopropylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide;
4-(3-chloro-4-(methylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide; and
N6-methoxy-4-(3-chloro-4-(((ethylamino)carbonyl)amino)phenoxy)-7-methoxy-6-quinolinecarboxamide,

a pharmacologically acceptable salt thereof or a solvate thereof.

75. A pharmaceutical composition according to Claim 61, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide, a pharmacologically acceptable salt thereof or a solvate thereof.

76. A pharmaceutical composition according to Claim 61, wherein the compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof is methanesulfonate of 4-(3-chloro-4-(cyclopropylaminocarbonyl)aminophenoxy)-7-methoxy-6-quinolinecarboxamide.

77. A pharmaceutical composition according to any one of Claims 61-76, wherein the substance having a c-kit kinase-inhibiting activity is at least one compound selected from the group consisting of:

(1) 4-(4-methylpiperazine-1-ylmethyl)-N-[4-methyl-3-[4-(3-pyridyl)pyrimidine-2-ylamino]phenyl]benzenamide;
(2) 3-[(2,4-dimethylpyrrole-5-yl)methylene]-2-indolinone;
(3) (Z)-3-[(2,4-dimethyl-5-(2-oxo-1,2-dihydroindole-3-ylidenemethyl)-1H-pyrrole-3-yl)-propionicacid;
(4) 5-(5-fluoro-2-oxo-1,2-dihydroindole-3-ylidenemethyl)-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide;
(5) N-{2-chloro-4-[(6,7-dimethoxy-4-quinazolinyl)oxy]phenyl}-N'-propylurea;
(6) 1-(4-chloroanilino)-4-(4-pyridylmethyl)phthalazine;
(7) N-{2-chloro-4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl)-N'-(5-methyl-3-isoxazolyl)urea;
(8) 4-[(4-fluoro-2-methylindole-5-yl)oxy]-6-methoxy-7-[3-(pyrrolidine-1-yl)propoxy]quinazoline;
(9) 6-[2-(methylcarbamoyl)phenylsulfanil]-3-E-[2-(pyridine-2-yl)ethenyl]indazole;
(10) N-(3-trifluoromethyl-4-chlorophenyl)-N'-(4-(2-methylcarbamoylpyridine-4-yl)oxyphenyl)urea;
(11) [6-[4-[(4-ethylpiperazine-1-yl)methyl]phenyl]-7H-pyrrolo[2,3-d]pyrimidine-4-yl]-((R)-1-phenylethyl)amine;
(12) 6-(2,6-dichloro-phenyl)-2-(4-fluoro-3-methyl-phenylamino)-8-methyl8H-pyrido[2,3-d]pyrimidine-7-one;
(13) 6-(2,6-dichlorophenyl)-8-methyl-2-(3-methylsulfanilphenylamino)-8H-pyrido[2,3-/d/]pyrimidine-7-one;
(14) 4-[6-methoxy-7-(3-piperidine-1-yl-propoxy)quinazoline-4-yl]piperazine-1-carboxylic acid(4-isopropoxyphenyl)amide; and
(15) N-(2-chloro-6-methylphenyl)-2-[[6-[4-(2-hydroxyethyl)piperazine-1-yl]-2-methylpyrimidine-4-yl] amino]thiazole-5-carboxamide,

a pharmacologically acceptable salt thereof or a solvate thereof.

78. A pharmaceutical composition according to any one of Claims 61-76, wherein the substance having a c-kit kinase-inhibiting activity is 4-(4-methylpiperazine-1-ylmethyl)-N-[4-methyl-3-[4-(3-pyridyl)pyrimidine-2-ylamino]phenyl]benzenamide, a pharmacologically acceptable salt thereof, or a solvate thereof.

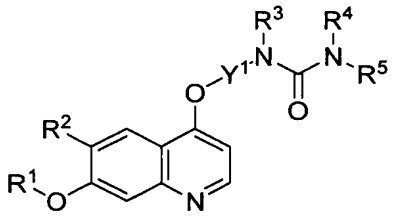
79. A pharmaceutical composition according to any one of Claims 61-76, wherein the substance having a c-kit kinase-

inhibiting activity is an anti-c-kit kinase antibody.

80. A pharmaceutical composition according to any one of Claims 61-79, wherein the pharmaceutical composition is a pharmaceutical composition for cancer treatment.

81. A method for treating cancer comprising administering an effective amount of a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof and an effective amount of a substance having a c-kit kinase-inhibiting activity to a patient:

Formula (I)

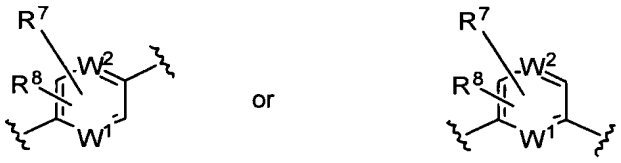


(I)

[wherein, R^1 represents group represented by Formula $-V^1-V^2-V^3$ (wherein, V^1 represents C_{1-6} alkylene group that may have a substituent; V^2 represents a single bond, an oxygen atom, a sulfur atom, carbonyl group, sulfinyl group, sulfonyl group, group represented by Formula $-CONR^6-$, group represented by Formula $-SO_2NR^6-$, group represented by Formula $-NR^6SO_2-$, group represented by Formula $-NR^6CO-$ or group represented by Formula $-NR^6-$ (wherein, R^6 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent or C_{3-8} cycloalkyl group that may have a substituent); V^3 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent);

R^2 represents cyano group, C_{1-6} alkoxy group that may have a substituent, carboxyl group, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{a11}V^{a12}$ (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent);

Y^1 represents group represented by Formula

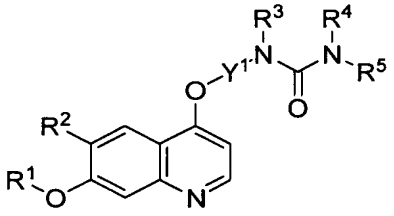


(wherein, R^7 and R^8 each independently represent a hydrogen atom, a halogen atom, cyano group, nitro group, amino group, C_{1-6} alkyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{1-6} alkoxy group that may have a substituent, C_{1-6} alkylthio group that may have a substituent, formyl group, C_{2-7} acyl group that may have a substituent, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{d1}V^{d2}$ (wherein, V^{d1} and V^{d2} each independently represent a hydrogen atom or C_{1-6} alkyl group that may have a substituent);

W^1 and W^2 each independently represent a carbon atom or a nitrogen atom that may have a substituent);
R^3 and R^4 each independently represent a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{2-7} acyl group that may have a substituent or C_{2-7} alkoxycarbonyl group that may have a substituent;
R^5 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent and 3-10-membered nonaromatic heterocyclic group that may have a substituent].

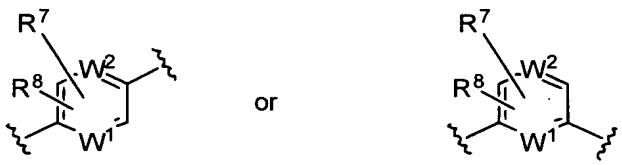
82. Use of a compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof for producing a pharmaceutical composition in combination with a substance having a c-kit kinase-inhibiting activity:

Formula (I)



(I)

[wherein, R^1 represents group represented by Formula $-V^1-V^2-V^3$ (wherein, V^1 represents C_{1-6} alkylene group that may have a substituent; V^2 represents a single bond, an oxygen atom, a sulfur atom, carbonyl group, sulfinyl group, sulfonyl group, group represented by Formula $-CONR^6-$, group represented by Formula $-SO_2NR^6-$, group represented by Formula $-NR^6SO_2-$, group represented by Formula $-NR^6CO-$ or group represented by Formula $-NR^6-$ (wherein, R^6 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent or C_{3-8} cycloalkyl group that may have a substituent); V^3 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent);
R^2 represents cyano group, C_{1-6} alkoxy group that may have a substituent, carboxyl group, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{a11}V^{a12}$ (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent);
Y^1 represents group represented by Formula

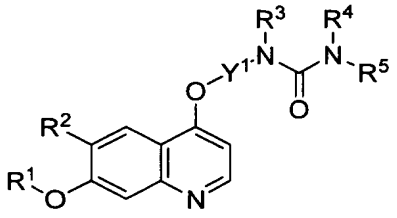


(wherein, R^7 and R^8 each independently represent a hydrogen atom, a halogen atom, cyano group, nitro

group, amino group, C_{1-6} alkyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{1-6} alkoxy group that may have a substituent, C_{1-6} alkylthio group that may have a substituent, formyl group, C_{2-7} acyl group that may have a substituent, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{d1}V^{d2}$ (wherein, V^{d1} and V^{d2} each independently represent a hydrogen atom or C_{1-6} alkyl group that may have a substituent);
W^1 and W^2 each independently represent a carbon atom or a nitrogen atom that may have a substituent);
R^3 and R^4 each independently represent a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{2-7} acyl group that may have a substituent or C_{2-7} alkoxycarbonyl group that may have a substituent;
R^5 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent].

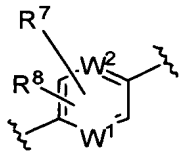
83. A compound represented by Formula (I), a pharmacologically acceptable salt thereof or a solvate thereof for providing a pharmaceutical composition in combination with a substance having a c-kit kinase-inhibiting activity:

Formula (I)

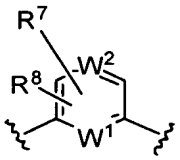


(I)

[wherein, R^1 represents group represented by Formula $-V^1-V^2-V^3$ (wherein, V^1 represents C_{1-6} alkylene group that may have a substituent; V^2 represents a single bond, an oxygen atom, a sulfur atom, carbonyl group, sulfinyl group, sulfonyl group, group represented by Formula $-CONR^6-$, group represented by Formula SO_2NR^6-, group represented by Formula $-NR^6SO_2-$, group represented by Formula $-NR^6CO-$ or group represented by Formula $-NR^6-$ (wherein, R^6 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent or C_{3-8} cycloalkyl group that may have a substituent); V^3 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent);
R^2 represents cyano group, C_{1-6} alkoxy group that may have a substituent, carboxyl group, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{a11}V^{a12}$ (wherein, V^{a11} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent; V^{a12} represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent, 3-10-membered nonaromatic heterocyclic group that may have a substituent, hydroxyl group, C_{1-6} alkoxy group that may have a substituent or C_{3-8} cycloalkoxy group that may have a substituent);
Y^1 represents group represented by Formula



or



(wherein, R^7 and R^8 each independently represent a hydrogen atom, a halogen atom, cyano group, nitro group, amino group, C_{1-6} alkyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{1-6} alkoxy group that may have a substituent, C_{1-6} alkylthio group that may have a substituent, formyl group, C_{2-7} acyl group that may have a substituent, C_{2-7} alkoxycarbonyl group that may have a substituent or group represented by Formula $-CONV^{d1}V^{d2}$ (wherein, V^{d1} and V^{d2} each independently represent a hydrogen atom or C_{1-6} alkyl group that may have a substituent);
W^1 and W^2 each independently represent a carbon atom or a nitrogen atom that may have a substituent);
R^3 and R^4 each independently represent a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{2-7} acyl group that may have a substituent or C_{2-7} alkoxycarbonyl group that may have a substituent;
R^5 represents a hydrogen atom, C_{1-6} alkyl group that may have a substituent, C_{2-6} alkenyl group that may have a substituent, C_{2-6} alkynyl group that may have a substituent, C_{3-8} cycloalkyl group that may have a substituent, C_{6-10} aryl group that may have a substituent, 5-10-membered heteroaryl group that may have a substituent or 3-10-membered nonaromatic heterocyclic group that may have a substituent].

Fig. 1

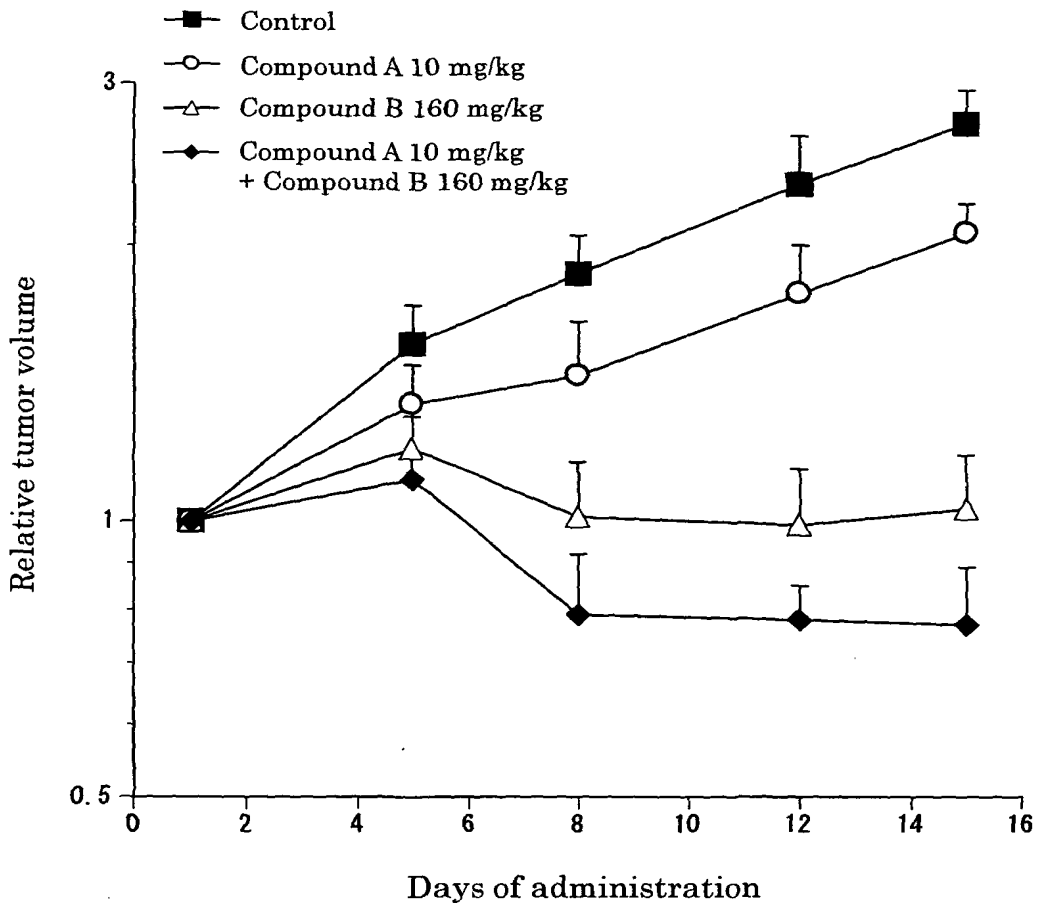
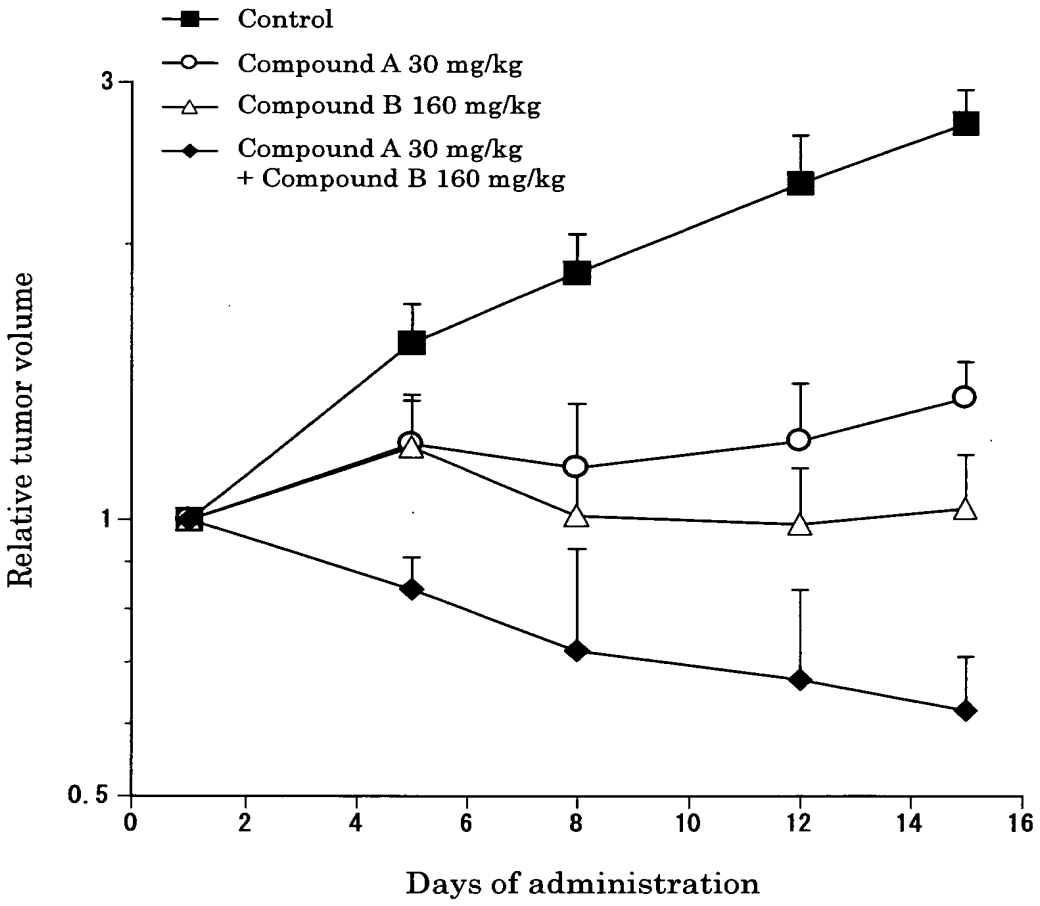

Control
Compound A 10 mg/kg
Compound B 160 mg/kg
Compound A 10 mg/kg
+ Compound B 160 mg/kg
Relative tumor volume
3
1
0.5
0
2
4
6
8
10
12
14
16
Days of administration

Fig. 2


Control
Compound A 30 mg/kg
Compound B 160 mg/kg
Compound A 30 mg/kg
+ Compound B 160 mg/kg
Relative tumor volume
3
1
0.5
0
2
4
6
8
10
12
14
16
Days of administration

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2006/322516

A. CLASSIFICATION OF SUBJECT MATTER
See extra sheet.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K31/47, A61K31/404, A61K31/4409, A61K31/4439, A61K31/4709, A61K31/502, A61K31/506, A61K31/517, A61K31/519, A61K31/5377, A61K39/395, A61K45/00, A61P35/00, A61P43/00, C07D215/48

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Jitsuyo Shinan Koho	1922-1996	Jitsuyo Shinan Toroku Koho	1996-2007
Kokai Jitsuyo Shinan Koho	1971-2007	Toroku Jitsuyo Shinan Koho	1994-2007

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
REGISTRY(STN), CAplus(STN)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	WO 2002/032872 A1 (Eisai Co., Ltd.), 25 April, 2002 (25.04.02), Full text; particularly, Claims; examples & JP 2002-536056 A & EP 1415987 A1 & US 2004/053908 A1 & CN 1478078 A & KR 2003040552 A	61-80,83 1-60,82
X Y	WO 2004/080462 A1 (Eisai Co., Ltd.), 23 September, 2004 (23.09.04), Full text; particularly, Claims; examples & JP 2005-503539 A & EP 1604665 A1 & US 2004/253205 A1	61-80,83 1-60,82
X Y	WO 2005/063713 A (Eisai Co., Ltd.), 14 July, 2005 (14.07.05), Full text; particularly, Claims; examples & EP 1698623 A1 & NO 200603383 A	61-80,83 1-60,82

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
04 January, 2007 (04.01.07)	23 January, 2007 (23.01.07)
Name and mailing address of the ISA/ Japanese Patent Office Facsimile No.	Authorized officer Telephone No.

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2006/322516

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	JP 2004-531549 A (Novartis AG.), 14 October, 2004 (14.10.04), Full text; particularly, Claims; Par. Nos. [0002], [0019], [0020] & WO 2002/092091 A1 & EP 1392313 A1 & US 2004/167134 A1 & CN 1700917 A & KR 2003094415 A	1-60,82
Y	WO 2005/027972 A2 (NOVARTIS PHARMA GMBH), 31 March, 2005 (31.03.05), Full text; particularly, Claims; page 8, lines 1 to 3 & EP 1682181 A2 & NO 200601777 A	1-60,82
Y	JP 2005-520834 A (Dana-Farber Cancer Institute, Inc.), 14 July, 2005 (14.07.05), Full text; particularly, Par. No. [0028] & WO 2003/079020 A2 & EP 1488239 A2 & US 2005/233991 A1	1-60,82

Form PCT/ISA/210 (continuation of second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2006/322516

Continuation of A. CLASSIFICATION OF SUBJECT MATTER
(International Patent Classification (IPC))

A61K31/47(2006.01)i, *A61K31/404*(2006.01)i, *A61K31/4409*(2006.01)i, *A61K31/4439*(2006.01)i, *A61K31/4709*(2006.01)i, *A61K31/502*(2006.01)i, *A61K31/506*(2006.01)i, *A61K31/517*(2006.01)i, *A61K31/519*(2006.01)i, *A61K31/5377*(2006.01)i, *A61K39/395*(2006.01)i, *A61K45/00*(2006.01)i, *A61P35/00*(2006.01)i, *A61P43/00*(2006.01)i, *C07D215/48*(2006.01)i

(According to International Patent Classification (IPC) or to both national classification and IPC)

Form PCT/ISA/210 (extra sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2006/322516

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [x] Claims Nos.: 81
because they relate to subject matter not required to be searched by this Authority, namely:
Claim 81 pertains to methods for treatment of the human body by therapy.

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

the

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, payment of a protest fee..

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet (2)) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/JP2006/322516

<Subject of search>

There is a term "a substance having a c-kit kinase-inhibiting activity" in claims 1, 21, 41, 61, 82 and 83. However, it appears that those substances which are supported by the description in the meaning within PCT Article 6 and disclosed in the meaning within PCT Article 5 are limited to a specific, extremely small part of the compounds having the property (e.g., imatinib).

With respect to the property "a substance having a c-kit kinase-inhibiting activity", even though the common technical knowledge at the time of the filing of the present application is taken into the consideration, it appears that the scope of the compound having the property cannot be specified.

Such being the case, the search was made on the relationship between a c-kit kinase-inhibiting activity and a compound of the formula (I) and also made on a combination of imatinib that is a compound specifically cited in the description as "a substance having a c-kit kinase-inhibiting activity" and specified in claims 18 or 19 or the like or an anti-c-kit antibody and a compound of the formula (I).

REFERENCES CITED IN THE DESCRIPTION

This list of references cited by the applicant is for the reader's convenience only. It does not form part of the European patent document. Even though great care has been taken in compiling the references, errors or omissions cannot be excluded and the EPO disclaims all liability in this regard.

Patent documents cited in the description

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- WO 2005063713 A **[0006] [0065] [0065] [0116]**
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- WO 9835958 A **[0066]**
- WO 2002088110 A **[0066]**
- WO 0047212 A **[0066]**
- WO 01002369 A **[0066]**
- WO 0042012 A **[0066]**

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